

STIC COMPOUND / METHOD SEARCH

schlapkohl - 10 / 716062

Page 1

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(FILE 'HOME' ENTERED AT 06:27:59 ON 09 FEB 2006)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 06:28:46 ON 09 FEB 2006

L1 2 S US20040082515/PN OR US2003-716062#/AP, PRN
E CLACKSON T/AU
L2 57 S E3, E5-E9
E GILMAN M/AU
L3 74 S E3, E8, E15, E17, E18
E HOLT D/AU
L4 36 S E3, E4
L5 103 S E45-E48
E KEENAN T/AU
L6 46 S E3, E12-E14
E ROZAMUS L/AU
L7 25 S E3-E6
E YANG W/AU
L8 1052 S E3-E30
L9 448 S YANG WU?/AU
E ARIAD/PA, CS
L10 185 S E3-E29
SEL RN L1

FILE 'REGISTRY' ENTERED AT 06:31:55 ON 09 FEB 2006

L11 133 S E1-E133
E NC4-OC5-NC2OC21OC3/ES
L12 9 S E3
E NC5-OC5-NC2OC21OC3/ES
L13 1186 S E3
L14 8 S L12 NOT RPS/CI
L15 1185 S L13 NOT RPS/CI
L16 37 S L11 AND L14, L15
L17 24 S L11 NOT (L16 OR SQL/FA)
L18 13 S L17 AND NR>=3
L19 11 S L18 AND NC5-OC5-NC2OC13OC3/ES
L20 72 S L11 NOT L16-L19

FILE 'HCAPLUS' ENTERED AT 06:45:55 ON 09 FEB 2006

L21 10 S L14
L22 3544 S L15
L23 3298 S L16
L24 3547 S L21-L23
L25 892 S L24 AND (PY<=1996 OR PRY<=1996 OR AY<=1996)
L26 17 S L1-L10 AND L25
L27 827 S L25 AND (GENETIC? OR BIOMOLECUL? OR BIOCHEM?)/SC, SX
E CHIMER/CT
L28 5671 S E11-E19
E E11+ALL
L29 11128 S E3+OLD, NT
E E18+ALL
L30 6790 S E1+OLD, NT
E CHIMERIC PROTEIN/CT
E E8+ALL
L31 17057 S E2
E E2+ALL
L32 20620 S E2+OLD, NT
E FUSION/CT
L33 1 S E33

jan delaval - 9 february 2006

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L34      17058 S E34-E52
          E PROTEIN MOTIF/CT
L35      66071 S E4-E40
          E E4+ALL
L36      69084 S E4+NT
          E GENETIC ENGINEERING/CT
          E E3+ALL
L37      103253 S E2+NT
L38      5093 S E18+OLD,NT
          E E1+ALL
L39      346300 S E1+NT
L40      130625 S E93(L)EXPRESS?
          E DNA/CT
L41      331318 S E3+OLD,NT
          E E3+ALL
L42      742161 S E3+OLD,NT OR E171+OLD,NT OR E172+OLD,NT OR E173+OLD,NT
          E CELL PROLIFERATION/CT
L43      78464 S E3-E11
          E E3+ALL
          E RECOMBIN/CT
L44      46528 S E49-E77
          E E49+ALL
L45      47814 S E1+NT
L46      87446 S E7+OLD,NT OR E9+OLD,NT
          E E9+ALL
          E HYBRIDIZATION/CT
          E E3+ALL
L47      82 S E1
          E E4+ALL
L48      51541 S E2+OLD,NT OR E11+OLD,NT
          E E11+ALL
L49      29988 S E3+OLD,NT
L50      16490 S E21+OLD,NT
L51      132 S L27 AND L28-L50
L52      33 S L51 AND (FKBP OR FRB)
L53      83 S L51 AND (FK506? OR FK 506)
L54      33 S L52 AND L53
L55      33 S L52,L54

FILE 'REGISTRY' ENTERED AT 07:04:29 ON 09 FEB 2006
L56      1 S RAPAMYCIN/CN
L57      1192 S L14,L15,L16 NOT L56

FILE 'HCAPLUS' ENTERED AT 07:04:56 ON 09 FEB 2006
L58      666 S L57
L59      152 S L58 AND (PY<=1996 OR PRY<=1996 OR AY<=1996)
L60      10 S L59 AND L28-L50
L61      139 S L59 AND (GENETIC? OR BIOMOLECUL? OR BIOCHEM?)/SC,SX
L62      8 S L60 AND L61
L63      18 S L1-L10 AND L58
L64      11 S L59 AND L63
L65      11 S L64 AND L60-L62
          SEL DN AN 3 5 6 7 8 9
L66      5 S L65 NOT E1-E18
L67      3 S L66 NOT PREPARATION/TI
L68      5 S L62 NOT L64
L69      3 S L68 AND (PROTEIN? OR DEOXYRIBONUCLEIC? OR RIBONUCLEIC?)/CW,C
L70      2 S L69 NOT CYCLOPHILINS
L71      9 S L60,L63 NOT L64-L70
          SEL AN DN 3 8

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L72      2 S L71 AND E19-E24
L73     13 S L59 AND (?FKBP? OR FRB?)
L74      5 S L73 AND L67,L70,L72
L75      8 S L73 NOT L74
L76      7 S L67,L70,L72,L74
L77      6 S L76 NOT 142:291846/DN
L78      6 S L59 AND (FUSION OR ?CHIMER?)
L79      5 S L78 NOT 143:32417/DN
L80      6 S L77,L79
L81      6 S L80 AND L1-L10,L21-L55,L58-L80
L82      6 S L81 AND (FUSION OR ?CHIMER? OR ?PROTEIN? OR ?PEPTIDE? OR BIND
          SEL HIT RN

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FILE 'REGISTRY' ENTERED AT 07:21:05 ON 09 FEB 2006

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L83      166 S E25-E190
          SAV L83 SCHLAP716/A
L84     1193 S L14-L16
          SAV L84 SCHLAP716A/A

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=> fil hcaplus

FILE 'HCAPLUS' ENTERED AT 07:22:03 ON 09 FEB 2006

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FILE COVERS 1907 - 9 Feb 2006 VOL 144 ISS 7

FILE LAST UPDATED: 8 Feb 2006 (20060208/ED)

New CAS Information Use Policies, enter HELP USAGETERMS for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L82  ANSWER 1 OF 6  HCAPLUS  COPYRIGHT 2006 ACS on STN
AN   2001:152693  HCAPLUS
DN   134:193290
ED   Entered STN:  02 Mar 2001
TI   Synthesis and biological activity of 28-epirapalogs with reduced
      immunosuppressive activity for multimerizing chimeric
      proteins
IN   Yang, Wu; Digits, Cheryl A.; Rozamus, Leonard;
      Holt, Dennis A.
PA   Ariad Gene Therapeutics, Inc., USA
SO   PCT Int. Appl., 96 pp.
      CODEN: PIXXD2
DT   Patent
LA   English

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IC ICM C07D0498-18
 ICS A61K0031-407; A61K0031-439; A61P0031-00; A61P0037-06; C07B0055-00;
 C07K0014-47; C12N0015-12; C12N0015-62; C07C0045-67; C07D0498-18;
 C07D0311-00; C07D0273-00; C07D0221-00; C07D0498-18; C07D0311-00;
 C07D0273-00; C07D0209-00

CC 26-6 (Biomolecules and Their Synthetic Analogs)
 Section cross-reference(s): 1, 9

FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 2001014387	A1	20010301	WO 2000-US23334	20000824
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
CA 2383451	AA	20010301	CA 2000-2383451	20000824
EP 1212331	A1	20020612	EP 2000-959391	20000824
EP 1212331	B1	20040421		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
AT 264863	E	20040515	AT 2000-959391	20000824
ES 2219388	T3	20041201	ES 2000-959391	20000824
AU 783158	B2	20050929	AU 2000-70725	20000824
US 2006025356	A1	20060202	US 2005-229992	20050919
PRAI US 1999-150447P	P	19990824		
US 2000-645967	A1	20000824		
WO 2000-US23334	W	20000824		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 2001014387	ICM	C07D0498-18
	ICS	A61K0031-407; A61K0031-439; A61P0031-00; A61P0037-06; C07B0055-00; C07K0014-47; C12N0015-12; C12N0015-62; C07C0045-67; C07D0498-18; C07D0311-00; C07D0273-00; C07D0221-00; C07D0498-18; C07D0311-00; C07D0273-00; C07D0209-00
	IPCI	C07D0498-18 [ICM,7]; A61K0031-407 [ICS,7]; A61K0031-439 [ICS,7]; A61P0031-00 [ICS,7]; A61P0037-06 [ICS,7]; C07B0055-00 [ICS,7]; C07K0014-47 [ICS,7]; C12N0015-12 [ICS,7]; C12N0015-62 [ICS,7]; C07C0045-67 [ICS,7]; C07D0498-18 [ICS,7]; C07D0311-00 [ICS,7]; C07D0273-00 [ICS,7]; C07D0221-00 [ICS,7]; C07D0209-00 [ICS,7]
	ECLA	A61K048/00; C07D498/18+311C+273D+221C; C07D498/18+311C+273D+209C; C12N009/12B1
CA 2383451	IPCI	C07D0498-18 [ICM,7]; C07B0055-00 [ICS,7]; C07D0209-00 [ICS,7]; C07D0221-00 [ICS,7]; C07D0273-00 [ICS,7]; C07D0311-00 [ICS,7]; A61P0031-00 [ICS,7]; A61P0037-06 [ICS,7]; C12N0015-12 [ICS,7]; A61K0031-407 [ICS,7]; A61K0031-439 [ICS,7]; C07K0014-47 [ICS,7]; C12N0015-62 [ICS,7]; C07C0045-67 [ICS,7]
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AT 264863 IPCI C07D0498-18 [ICM,7]; A61K0031-407 [ICS,7]; A61K0031-439 [ICS,7]; A61P0031-00 [ICS,7]; A61P0037-06 [ICS,7]; C07B0055-00 [ICS,7]; C07K0014-47 [ICS,7]; C12N0015-12 [ICS,7]

ES 2219388 IPCI C07D0498-18 [ICM,7]; A61K0031-407 [ICS,4]; A61K0031-439 [ICS,4]; A61P0031-00 [ICS,4]; A61P0037-06 [ICS,4]; C07B0055-00 [ICS,7]; C07K0014-47 [ICS,4]; C12N0015-12 [ICS,4]; C12N0015-62 [ICS,4]; C07C0045-67 [ICS,7]; C07D0311-00 [ICS,7]; C07D0273-00 [ICS,7]; C07D0221-00 [ICS,7]; C07D0209-00 [ICS,7]

AU 783158 IPCI C07D0498-18 [ICM,7]; A61K0031-407 [ICS,7]; A61K0031-439 [ICS,7]; A61P0031-00 [ICS,7]; A61P0037-06 [ICS,7]; C07B0055-00 [ICS,7]; C07C0045-67 [ICS,7]; C07D0209-00 [ICS,7]; C07D0221-00 [ICS,7]; C07D0273-00 [ICS,7]; C07D0311-00 [ICS,7]; C07K0014-47 [ICS,7]; C12N0015-12 [ICS,7]; C12N0015-62 [ICS,7]

US 2006025356 IPCI A61K0031-4745 [I,A]; C07D0491-14 [I,A]
NCL 514/029.000; 514/291.000; 540/456.000; 540/457.000

OS MARPAT 134:193290

AB Methods and materials involving synthesis of **28-epirapamycin** analogs are disclosed. Thus, **28-epirapamycin** is synthesized via cleavage of **rapamycin** with titanium tetrakisoperoxide and retro aldol macrocyclization and analogs are prepared by modification at C7 and C43. These analogs have reduced immunosuppressive activity and comparative data for FKRB **binding**, activity in cellular transcription assay and activity in mouse splenocyte assay are given.

ST **rapamycin** epimer analog prepn; **epirapamycin**
chimeric protein FKRB domain biol regulation

IT **Proteins, specific or class**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(**FKBP** (FK 506-binding protein),
chimeric proteins with effector domain-containing
proteins; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and
rapamycin analogs lacking immunosuppressive action)

IT **Fusion proteins (chimeric proteins)**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(**FKBP** and **FRB** domain and effector domain-containing;
regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)

IT **Protein motifs**
(**FKBP** and **FRB** domains; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)

IT **Proteins, specific or class**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(**FKBP** protein-**rapamycin**-binding
(**FRB**) domain-containing, **chimeric proteins** containing; regulation of biol. events using **chimeric**

- proteins containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT Transcription, **genetic**
(activation of; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT **Chimeric gene**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(**animal**, **FKBP** and **FRB** domain and effector domain-containing **protein**-encoding; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT **DNA**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(**binding** of; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT **Gene, animal**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(**chimeric**, **FKBP** and **FRB** domain and effector domain-containing **protein**-encoding; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT Transcription factors
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(**fusion proteins** with **FRB**-containing **proteins**; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT Cell differentiation
(inducers; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT Growth factor receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(kinase, activation of; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT Immunosuppressants
(reduced activity; synthesis and biol. activity of 28-epirapalogs with reduced immunosuppressive activity for multimerizing **chimeric proteins**)
- IT Apoptosis
Cell proliferation
(stimulation of; regulation of biol. events using **chimeric**

- proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT Epimerization
(synthesis and biol. activity of 28-epirapalogs with reduced immunosuppressive activity for multimerizing **chimeric proteins**)
- IT 147438-29-7P **253431-37-7P**, 29-**Epirapamycin**
253431-39-9P, 28,29-**Bisepirapamycin**
RL: BYP (Byproduct); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(epimerization; synthesis and biol. activity of 28-epirapalogs with reduced immunosuppressive activity for multimerizing **chimeric proteins**)
- IT 56-84-8, Aspartic acid, biological studies 56-85-9, Glutamine, biological studies 60-18-4, Tyrosine, biological studies 63-91-2, Phenylalanine, biological studies 72-19-5, Threonine, biological studies 73-22-3, Tryptophan, biological studies
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(replacement amino acid in **FRB** domain)
- IT **328059-76-3P 328059-77-4P 328059-78-5P**
328059-79-6P 328059-80-9P 328059-81-0P
328059-82-1P 328059-83-2P 328059-84-3P
328059-85-4P 328059-86-5P 328059-87-6P
328059-88-7P 328059-89-8P 328059-90-1P
328059-91-2P 328059-92-3P 328059-93-4P
328059-94-5P 328059-95-6P 328059-96-7P
328059-97-8P 328059-98-9P 328059-99-0P
328060-00-0P 328060-01-1P 328060-02-2P
328060-03-3P 328060-04-4P 328060-05-5P
328060-06-6P 328060-07-7P 328060-08-8P
328060-09-9P 328060-10-2P 328060-11-3P
328060-12-4P 328060-13-5P 328060-14-6P
328060-15-7P 328060-16-8P 328060-17-9P
328060-18-0P 328060-19-1P 328060-20-4P
328060-21-5P 328060-22-6P 328060-23-7P
328060-24-8P 328060-25-9P 328060-26-0P
328060-27-1P 328060-28-2P 328060-29-3P
328060-30-6P 328060-31-7P 328060-32-8P
328060-33-9P 328060-34-0P 328060-35-1P
328060-36-2P 328060-37-3P 328060-38-4P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(synthesis and biol. activity of 28-epirapalogs with reduced immunosuppressive activity for multimerizing **chimeric proteins**)
- IT 546-68-9, Titanium tetraisopropoxide
RL: CAT (Catalyst use); USES (Uses)
(synthesis and biol. activity of 28-epirapalogs with reduced immunosuppressive activity for multimerizing **chimeric proteins**)
- IT 100-52-7, Benzaldehyde, reactions 333-27-7, Methyl triflate
41029-45-2, Allyl triflate
RL: RCT (Reactant); RACT (Reactant or reagent)
(synthesis and biol. activity of 28-epirapalogs with reduced immunosuppressive activity for multimerizing **chimeric proteins**)
- IT 253431-42-4P
RL: SPN (Synthetic preparation); PREP (Preparation)

(synthesis and biol. activity of 28-epirapalogs with reduced immunosuppressive activity for multimerizing **chimeric proteins**)

IT **53123-88-9, Rapamycin**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); THU (Therapeutic use); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(tautomer; synthesis and biol. activity of 28-epirapalogs with reduced immunosuppressive activity for multimerizing **chimeric proteins**)

IT **253431-35-5P, 28-Epirapamycin**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(tautomer; synthesis and biol. activity of 28-epirapalogs with reduced immunosuppressive activity for multimerizing **chimeric proteins**)

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD
RE

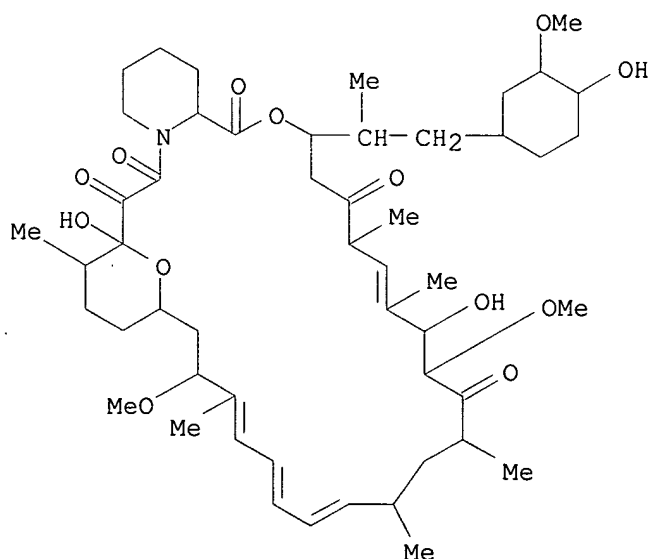
- (1) American Home Products Corp; WO 9809972 A 1998 HCAPLUS
- (2) Ariad Gene Therapeutics; WO 9641865 A 1996 HCAPLUS
- (3) Ariad Gene Therapeutics; WO 9936553 A 1999 HCAPLUS
- (4) Hayward, C; Journal of the American Chemical Society 1993, V115(20), P9345 HCAPLUS
- (5) Mahrwald, R; Synthesis 1990, 7, P592 HCAPLUS
- (6) Swiss, K; Journal of Organic Chemistry 1991, V56(21), P5978 HCAPLUS
- (7) Takasago International Corp; EP 0614871 A 1994 HCAPLUS
- (8) Yang, W; Organic Letters 1999, V1(12), P2033 HCAPLUS

IT **253431-37-7P, 29-Epirapamycin**

RL: BYP (Byproduct); PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)
(epimerization; synthesis and biol. activity of 28-epirapalogs with reduced immunosuppressive activity for multimerizing **chimeric proteins**)

RN 253431-37-7 HCAPLUS

CN Rapamycin, (32S)- (9CI) (CA INDEX NAME)



L82 ANSWER 2 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
 AN 2001:111506 HCAPLUS
 DN 134:173056
 ED Entered STN: 14 Feb 2001
 TI Regulation of biol. events using novel compds. comprizing **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action
 IN Clarkson, Timothy P.; Gilman, Michael Z.; Holt, Dennis A.; Keenan, Terence P.; Rozamus, Leonard; Yang, Wu
 PA Ariad Pharmaceuticals, Inc., USA
 SO U.S., 101 pp., Cont.-in-part of U.S. Ser. No. 791,044, abandoned.
 CODEN: USXXAM
 DT Patent
 LA English
 IC A61K0031-70; C12N0005-10
 INCL 514031000
 CC 1-12 (Pharmacology)
 Section cross-reference(s): 3, 9, 26

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	US 6187757	B1	20010213	US 1998-12097	19980122 <--
	WO 9641865	A1	19961227	WO 1996-US9948	19960607 <--
	W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
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	WO 9936553	A2	19990722	WO 1999-US178	19990115
	WO 9936553	A3	19991021		
	W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
	RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
	AU 9922132	A1	19990802	AU 1999-22132	19990115
	AU 755784	B2	20021219		
	EP 1045915	A2	20001025	EP 1999-902059	19990115
	R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
	JP 2002508971	T2	20020326	JP 2000-540254	19990115
	US 2002107189	A1	20020808	US 2001-781804	20010212 <--
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PRAI	US 1995-481941	B2	19950607	<--	
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CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
US 6187757	IC	A61K0031-70; C12N0005-10
	INCL	514031000
	IPCI	A61K0031-70; C12N0005-10
	IPCR	A61K0048-00 [N,A]; A61K0048-00 [N,C]; C07K0014-435 [I,C]; C07K0014-715 [I,A]; C12N0009-12 [I,A]; C12N0009-12 [I,C]; C12N0015-10 [I,A]; C12N0015-10 [I,C]; C12N0015-85 [I,A]; C12N0015-85 [I,C]
	NCL	514/031.000; 435/325.000; 435/355.000; 435/372.000; 435/372.300; 435/375.000
WO 9641865	ECLA	C07K014/715; C12N009/12B1; C12N015/10C6; C12N015/85 <--
	IPCI	C12N0005-10 [ICM,6]; C12N0009-90 [ICS,6]; C12N0015-12 [ICS,6]; C12N0015-10 [ICS,6]; C12N0015-31 [ICS,6]; C12N0015-62 [ICS,6]; C12N0015-63 [ICS,6]; C12N0015-85 [ICS,6]; C12N0015-86 [ICS,6]; C07K0014-395 [ICS,6]; C07K0014-47 [ICS,6]; C07K0014-715 [ICS,6]; C12Q0001-68 [ICS,6]; A01K0067-027 [ICS,6]
	IPCR	A61K0048-00 [N,A]; A61K0048-00 [N,C]; C07K0014-435 [I,C]; C07K0014-715 [I,A]; C12N0009-12 [I,A]; C12N0009-12 [I,C]; C12N0015-10 [I,A]; C12N0015-10 [I,C]; C12N0015-85 [I,A]; C12N0015-85 [I,C]
CA 2318402	ECLA	C07K014/715; C12N009/12B1; C12N015/10C6; C12N015/85 <--
	IPCI	C12N0015-62 [ICM,6]; C07K0019-00 [ICS,6]; C12N0009-12 [ICS,6]; C07D0498-18 [ICS,6]; C07K0014-47 [ICS,6]
WO 9936553	IPCI	C12N0015-62 [ICM,6]; C07K0019-00 [ICS,6]; C07K0014-47 [ICS,6]; C12N0009-12 [ICS,6]; C07D0498-18 [ICS,6]; C07D0498-18 [ICS,6]; C07D0273-00 [ICS,6]; C07D0311-00 [ICS,6]; C07D0221-00 [ICS,6]
	IPCR	C07D0498-00 [I,C]; C07D0498-18 [I,A]; C07K0014-005 [I,C]; C07K0014-035 [I,A]; C07K0014-37 [I,C]; C07K0014-395 [I,A]; C07K0014-435 [I,C]; C07K0014-47 [I,A]; C07K0014-705 [I,A]; C07K0014-725 [I,A]; C12N0009-12 [I,A]; C12N0009-12 [I,C]
	ECLA	C07D498/18+273D+311C+221C; C07K014/035; C07K014/395; C07K014/47; C07K014/705B12; C07K014/705R; C12N009/12B1
AU 9922132	IPCI	C12N0015-62 [ICM,6]; C07K0019-00 [ICS,6]; C07K0014-47 [ICS,6]; C12N0009-12 [ICS,6]; C07D0498-18 [ICS,6]
EP 1045915	IPCI	C12N0015-62 [ICM,6]; C07K0019-00 [ICS,6]; C07K0014-47 [ICS,6]; C12N0009-12 [ICS,6]; C07D0498-18 [ICA,6]
JP 2002508971	IPCI	C12N0015-09 [ICM,7]; A61K0031-436 [ICS,7]; A61K0048-00 [ICS,7]; A61P0037-06 [ICS,7]; C07D0498-18 [ICS,7]; C07K0014-00 [ICS,7]; C07K0019-00 [ICS,7]; C07D0273-00 [ICS,7]; C07D0311-00 [ICS,7]; C07D0221-00 [ICS,7]
US 2002107189	IPCI	A61K0038-17 [ICM,7]; C12P0021-02 [ICS,7]
	IPCR	A61K0048-00 [N,A]; A61K0048-00 [N,C]; C07D0498-00 [I,C]; C07D0498-18 [I,A]; C07K0014-005 [I,C]; C07K0014-035 [I,A]; C07K0014-37 [I,C]; C07K0014-395 [I,A]; C07K0014-435 [I,C]; C07K0014-47 [I,A]; C07K0014-705 [I,A]; C07K0014-715 [I,A]; C07K0014-725 [I,A]; C12N0009-12 [I,A]; C12N0009-12 [I,C]; C12N0015-10 [I,A]; C12N0015-10 [I,C]; C12N0015-85 [I,A]; C12N0015-85 [I,C]
	NCL	514/012.000
	ECLA	C07D498/18+273D+311C+221C; C07K014/035; C07K014/395; C07K014/47; C07K014/705B12; C07K014/705R; C07K014/715; C12N009/12B1; C12N015/10C6; C12N015/85 <--

US 2004082515 IPCI A61K0039-395 [ICM,7]; G01N0033-53 [ICS,7]
 IPCR A61K0048-00 [N,A]; A61K0048-00 [N,C]; C07D0498-00
 [I,C]; C07D0498-18 [I,A]; C07K0014-005 [I,C];
 C07K0014-035 [I,A]; C07K0014-37 [I,C]; C07K0014-395
 [I,A]; C07K0014-435 [I,C]; C07K0014-47 [I,A];
 C07K0014-705 [I,A]; C07K0014-715 [I,A]; C07K0014-725
 [I,A]; C12N0009-12 [I,A]; C12N0009-12 [I,C];
 C12N0015-10 [I,A]; C12N0015-10 [I,C]; C12N0015-85
 [I,A]; C12N0015-85 [I,C]
 NCL 514/012.000
 ECLA C07D498/18+273D+311C+221C; C07K014/035; C07K014/395;
 C07K014/47; C07K014/705B12; C07K014/705R; C07K014/715;
 C12N009/12B1; C12N015/10C6; C12N015/85 <--

OS MARPAT 134:173056

AB Materials and methods are disclosed for regulation of biol. events such as target **gene** transcription and growth, proliferation or differentiation of engineered cells. This invention provides methods and materials for multimerizing **chimeric proteins** in genetically engineered cells using improved **rapamycin** analogs (rapalog), preferably while avoiding the immunosuppressive effects of **rapamycin**. The genetically engineered cells contain one or more **recombinant** nucleic acid constructs encoding specialized **chimeric proteins** as described herein. Typically a first **chimeric protein** contains one or more **FKBP** domains which are capable of **binding** to an improved rapalog of this invention. This first **chimeric protein** is also referred to herein as an "**FKBP fusion protein**" and further comprises at least one **protein** domain heterologous to at least one of its **FKBP** domains. The complex formed by the **binding** of the **FKBP fusion protein** to the rapalog is capable of **binding** to a second **chimeric protein** which contains one or more **FRB** domains (the "**FRB fusion protein**"). The **FRB fusion protein** further comprises at least one **protein** domain heterologous to at least one of its **FRB** domains. In some embodiments, the **FKBP fusion protein** and the **FRB fusion protein** are different from one another. In other embodiments, however, the **FKBP fusion protein** is also an **FRB fusion protein**. In those embodiments, the **chimeric protein** comprises one or more **FKBP** domains as well as one or more **FRB** domains. In such cases, the first and second **chimeric proteins** may be the same **protein**, may be referred to as **FKBP-FRB fusion proteins** and contain at least one domain heterologous to the **FKBP** and/or **FRB** domains. The **chimeric proteins** may be readily designed, based on incorporation of appropriately chosen heterologous domains, such that their multimerization triggers one or more of a wide variety of desired biol. responses. The nature of the biol. response triggered by rapalog-mediated complexation is determined by the choice of heterologous domains in the **fusion proteins**. The heterologous domains are therefore referred to as "action" or "effector" domains. The genetically engineered cells for use in practicing this invention will contain one or more **recombinant** nucleic acid constructs encoding the **chimeric proteins**, and in certain applications, will further contain one or more accessory nucleic acid constructs, such as one or more target **gene** constructs.

ST **chimeric protein FKBP** domain
rapamycin analog biol regulation

- IT **Proteins, specific or class**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(FKBP (FK 506-binding protein), chimeric proteins with effector domain-containing proteins; regulation of biol. events using chimeric proteins containing FKBP and FRB domains and rapamycin analogs lacking immunosuppressive action)
- IT **Plasmids**
(FKBP and FRB domain and effector domain-containing protein-encoding; regulation of biol. events using chimeric proteins containing FKBP and FRB domains and rapamycin analogs lacking immunosuppressive action)
- IT **Fusion proteins (chimeric proteins)**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(FKBP and FRB domain and effector domain-containing; regulation of biol. events using chimeric proteins containing FKBP and FRB domains and rapamycin analogs lacking immunosuppressive action)
- IT **Protein motifs**
(FKBP and FRB domains; regulation of biol. events using chimeric proteins containing FKBP and FRB domains and rapamycin analogs lacking immunosuppressive action)
- IT **Proteins, specific or class**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(FKBP protein-rapamycin-binding (FRB) domain-containing, chimeric proteins containing; regulation of biol. events using chimeric proteins containing FKBP and FRB domains and rapamycin analogs lacking immunosuppressive action)
- IT **Gene, microbial**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(GAL4, chimeric gene with FRB-containing protein gene; regulation of biol. events using chimeric proteins containing FKBP and FRB domains and rapamycin analogs lacking immunosuppressive action)
- IT **Transcription factors**
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(GAL4, fusion proteins with FRB-containing proteins; regulation of biol. events using chimeric proteins containing FKBP and FRB domains and rapamycin analogs lacking immunosuppressive action)

- IT Transcription factors
 RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
 (NF- κ B (nuclear factor κ B), p65 subunit, **fusion proteins** with **FRB**-containing **proteins**; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT Transcription factors
 RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
 (VP16, **fusion proteins** with **FRB**-containing **proteins**; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT Transcription factors
 RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
 (ZFHD1, **fusion proteins** with **FRB**-containing **proteins**; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT Transcription, **genetic**
 (activation of; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT **Chimeric gene**
 RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
 (**animal**, **FKBP** and **FRB** domain and effector domain-containing **protein**-encoding; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT **DNA**
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (**binding** of; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT **Gene, animal**
 RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
 (**chimeric**, **FKBP** and **FRB** domain and effector domain-containing **protein**-encoding; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT **Gene**

- (**expression**, stimulation of; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT **Retroviral vectors**
(**fusion proteins** expression with; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT Transcription factors
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(**fusion proteins** with **FRB**-containing **proteins**; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT Cell differentiation
(inducers; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT Growth factor receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(kinase, activation of; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT Signal transduction, biological
(modulation of; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT Mutation
(of **FKBP** and **FRB** domain-containing **chimeric proteins**; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT **Genetic engineering**
Immunosuppressants
(regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT Apoptosis
Cell proliferation
(stimulation of; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT 127407-08-3
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(activation of; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)
- IT 326041-74-1P, **Protein** (plasmid pCGNN-2FHD1-3**FKBP**)
RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
(amino acid sequence; regulation of biol. events using **chimeric**

proteins containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)

IT 326041-75-2P 326041-76-3P 326041-77-4P 326041-78-5P 326041-79-6P
 326041-80-9P 326041-81-0P 326041-82-1P 326041-83-2P 326041-84-3P
 326041-85-4P 326041-86-5P 326041-87-6P 326041-88-7P 326041-89-8P
 326041-90-1P
 RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
 (mutant **FKBP12**-encoding; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)

IT 326041-91-2P 326041-92-3P 326041-93-4P 326041-94-5P 326041-95-6P
 326041-96-7P 326041-97-8P 326041-98-9P 326041-99-0P 326042-00-6P
 RL: BPN (Biosynthetic preparation); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PREP (Preparation); PROC (Process)
 (mutant **FRB** domain-containing **protein**-encoding; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)

IT 9002-72-6, Growth hormone
 RL: BPR (Biological process); BSU (Biological study, unclassified); MFM (Metabolic formation); BIOL (Biological study); FORM (Formation, nonpreparative); PROC (Process)
 (rapamycin-dependent production of; regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)

IT 67-63-0, 2-Propanol, biological studies 53123-88-9D, **Rapamycin**, analogs 157054-82-5 157054-84-7
 157182-35-9 157182-38-2 160349-48-4
 160401-32-1 167868-35-1 167868-36-2
 167938-80-9 202522-51-8 202522-52-9
 202583-23-1 202583-24-2
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)

IT 53123-88-9, **Rapamycin**
 RL: BPR (Biological process); BSU (Biological study, unclassified); RCT (Reactant); BIOL (Biological study); PROC (Process); RACT (Reactant or reagent)
 (regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)

IT 161754-08-1P 161754-09-2P 186757-66-4P
 186757-67-5P 186757-68-6P 186757-69-7P
 186757-70-0P 186757-71-1P 186757-72-2P
 186757-73-3P 186757-79-9P 186757-80-2P
 186757-81-3P 186794-75-2P 186794-97-8P
 202522-54-1P 202522-55-2P 202522-56-3P
 202522-57-4P 325963-20-0P 325963-21-1P
 326595-75-9P, AP 1491
 RL: BPR (Biological process); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
 (regulation of biol. events using **chimeric proteins**

containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)

IT 120-72-9, Indole, reactions 151-10-0, 1,3-Dimethoxybenzene 872-55-9, 2-Ethylthiophene 1689-78-7 2049-73-2, 1,3-Diethoxybenzene 69739-34-0, tert-Butyldimethylsilyl trifluoromethanesulfonate 74124-79-1, N,N'-Disuccinimidylcarbonate 104987-11-3, **FK506** 106754-95-4, 4'-(Aminomethyl)fluorescein

RL: RCT (Reactant); RACT (Reactant or reagent)
(regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)

IT 133941-75-0P **158472-50-5P** 161140-18-7P 161140-19-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)

IT **202522-60-9P**

RL: SPN (Synthetic preparation); PREP (Preparation)
(regulation of biol. events using **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)

IT 246862-98-6 325963-22-2 325963-23-3 326046-95-1, 54: PN: US6187757

SEQID: 7 unclaimed **DNA** 326047-04-5 326047-05-6 326047-06-7

326047-34-1 326047-35-2 326047-36-3 326047-37-4 326047-38-5

326047-39-6 326047-40-9 326047-41-0 326047-42-1 326047-43-2

326047-44-3 326047-45-4 326047-46-5 337792-90-2 337792-91-3

337792-92-4 337792-93-5 337792-94-6 337792-96-8 337792-97-9

337792-98-0 337792-99-1 337793-00-7 337793-01-8 337793-02-9

337793-03-0 337793-04-1

RL: PRP (Properties)
(unclaimed nucleotide sequence; regulation of biol. events using novel compds. comprizing **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)

IT 326047-33-0

RL: PRP (Properties)
(unclaimed **protein** sequence; regulation of biol. events using novel compds. comprizing **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)

IT 325963-24-4 325963-25-5

RL: PRP (Properties)
(unclaimed sequence; regulation of biol. events using novel compds. comprizing **chimeric proteins** containing **FKBP** and **FRB** domains and **rapamycin** analogs lacking immunosuppressive action)

RE.CNT 138 THERE ARE 138 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT 53123-88-9D, Rapamycin, analogs

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
 (Biological study); PROC (Process)
 (regulation of biol. events using **chimeric proteins**
 containing **FKBP** and **FRB** domains and **rapamycin**
 analogs lacking immunosuppressive action)

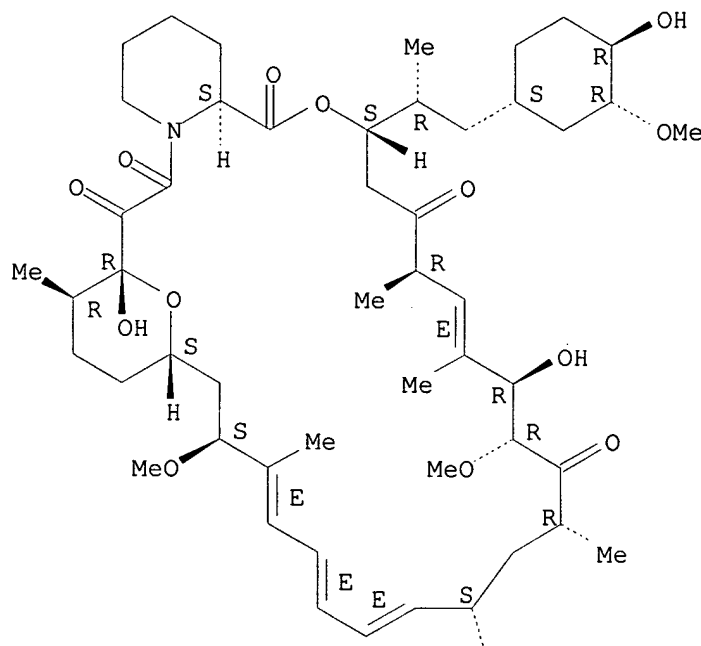
RN 53123-88-9 HCAPLUS

CN Rapamycin (9CI) (CA INDEX NAME)

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A



PAGE 2-A

Me

L82 ANSWER 3 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
 AN 1999:468639 HCAPLUS
 DN 131:112371
 ED Entered STN: 30 Jul 1999
 TI Regulation of biological events using **fusion proteins**

jan delaval - 9 february 2006

of rapamycin-binding proteins and rapamycin analogs

IN Clackson, Timothy P.; Gilman, Michael Z.; Holt, Dennis A.; Keenan, Terence P.; Rozamus, Leonard; Yang, Wu

PA Ariad Gene Therapeutics, Inc., USA

SO PCT Int. Appl., 155 pp.
CODEN: PIXXD2

DT Patent

LA English

IC ICM C12N0015-62
ICS C07K0019-00; C07K0014-47; C12N0009-12; C07D0498-18; C07D0498-18;
C07D0273-00; C07D0311-00; C07D0221-00

CC 3-1 (Biochemical Genetics)

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9936553	A2	19990722	WO 1999-US178	19990115
	WO 9936553	A3	19991021		
	W:	AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
	RW:	AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE			
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	CA 2318402	AA	19990722	CA 1999-2318402	19990115
	AU 9922132	A1	19990802	AU 1999-22132	19990115
	AU 755784	B2	20021219		
	EP 1045915	A2	20001025	EP 1999-902059	19990115
	R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
	JP 2002508971	T2	20020326	JP 2000-540254	19990115
PRAI	US 1998-71591P	P	19980115		
	US 1998-72016P	P	19980121		
	US 1998-12097	A	19980122		
	US 1998-72219P	P	19980122		
	US 1995-481941	B2	19950607	<--	
	US 1996-15502P	P	19960209	<--	
	WO 1996-US9948	A2	19960607	<--	
	US 1997-791044	A2	19970128		
	WO 1999-US178	W	19990115		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9936553	ICM	C12N0015-62
	ICS	C07K0019-00; C07K0014-47; C12N0009-12; C07D0498-18; C07D0498-18; C07D0273-00; C07D0311-00; C07D0221-00
	IPCI	C12N0015-62 [ICM,6]; C07K0019-00 [ICS,6]; C07K0014-47 [ICS,6]; C12N0009-12 [ICS,6]; C07D0498-18 [ICS,6]; C07D0498-18 [ICS,6]; C07D0273-00 [ICS,6]; C07D0311-00 [ICS,6]; C07D0221-00 [ICS,6]
	ECLA	C07D498/18+273D+311C+221C; C07K014/035; C07K014/395; C07K014/47; C07K014/705B12; C07K014/705R; C12N009/12B1
US 6187757	IPCI	A61K0031-70; C12N0005-10
	NCL	514/031.000; 435/325.000; 435/355.000; 435/372.000; 435/372.300; 435/375.000
	ECLA	C07K014/715; C12N009/12B1; C12N015/10C6; C12N015/85 <--

CA 2318402 IPCI C12N0015-62 [ICM,6]; C07K0019-00 [ICS,6]; C12N0009-12 [ICS,6]; C07D0498-18 [ICS,6]; C07K0014-47 [ICS,6]

AU 9922132 IPCI C12N0015-62 [ICM,6]; C07K0019-00 [ICS,6]; C07K0014-47 [ICS,6]; C12N0009-12 [ICS,6]; C07D0498-18 [ICS,6]

EP 1045915 IPCI C12N0015-62 [ICM,6]; C07K0019-00 [ICS,6]; C07K0014-47 [ICS,6]; C12N0009-12 [ICS,6]; C07D0498-18 [ICA,6]

JP 2002508971 IPCI C12N0015-09 [ICM,7]; A61K0031-436 [ICS,7]; A61K0048-00 [ICS,7]; A61P0037-06 [ICS,7]; C07D0498-18 [ICS,7]; C07K0014-00 [ICS,7]; C07K0019-00 [ICS,7]; C07D0273-00 [ICS,7]; C07D0311-00 [ICS,7]; C07D0221-00 [ICS,7]

OS MARPAT 131:112371

AB A method of regulating biol. processes using **fusion proteins** of **FK506-binding proteins** and regulatory **protein** is described. The method uses analogs of **rapamycin** to mediate the interaction between **FK506-binding domains** of **fusion proteins**. The method avoids the problems associated with immunosuppression by **rapamycins**. A series of analogs of **rapamycin** with substitutions at C7, C24, or C30 were prepared and tested for their **binding** to **FKBP**. Several series of **fusion proteins** containing **FK506-binding domains** and the **DNA-binding** or transcription-activating domains of a number of well characterized transcription factors (including GAL4, VP16, NFκB p65 subunit) were prepared by standard methods. **Fusion proteins** that could be activated by added **rapamycin** analogs were identified. Induction ratios of >104 were obtained. The use of these **fusion proteins** to direct expression of a human growth hormone **gene** in mice inoculated with cells carrying a **rapamycin** regulated expression system was demonstrated. Phage display libraries for use in optimization of **rapamycin binding** and responsiveness are described. Methods of using these **fusion proteins** to modulate receptor-dependent processes, especially signal transduction, are described.

ST **rapamycin binding protein fusion product; FK506 binding protein rapamycin binding domain; transcription factor rapamycin regulation FKBP fusion protein; apoptosis rapamycin regulation; signal transduction rapamycin regulation; gene expression rapamycin regulation**

IT **Proteins, specific or class**
 RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
 (FKBP (FK 506-binding protein), **fusion proteins**; regulation of biol. events using **fusion proteins** of **rapamycin-binding proteins** and **rapamycin** analogs)

IT **Proteins, specific or class**
 RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
 (FKBP-12 (FK 506-binding protein, 12,000-mol.-weight), **fusion protein** with GAL4; regulation of biol. events using **fusion proteins** of **rapamycin-binding proteins** and **rapamycin** analogs)

IT **Proteins, specific or class**
 RL: BPR (Biological process); BSU (Biological study, unclassified); BUU

(Biological use, unclassified); BIOL (Biological study); PROC (Process);
USES (Uses)

(FRAP (FK506:rapamycin-binding
protein), fusion proteins; regulation of
biol. events using fusion proteins of
rapamycin-binding proteins and
rapamycin analogs)

IT Transcription factors

RL: BPR (Biological process); BSU (Biological study, unclassified); BUU
(Biological use, unclassified); BIOL (Biological study); PROC (Process);
USES (Uses)

(GAL4, fusion protein with FKBP12;
regulation of biol. events using fusion proteins of
rapamycin-binding proteins and
rapamycin analogs)

IT Transcription factors

RL: BPR (Biological process); BSU (Biological study, unclassified); BUU
(Biological use, unclassified); BIOL (Biological study); PROC (Process);
USES (Uses)

(NF-κB (nuclear factor κB), p65 subunit, fusion
protein with FKBP; regulation of biol. events using
fusion proteins of rapamycin-
binding proteins and rapamycin analogs)

IT Transcription factors

RL: BPR (Biological process); BSU (Biological study, unclassified); BUU
(Biological use, unclassified); BIOL (Biological study); PROC (Process);
USES (Uses)

(VP16, fusion protein with FKBP12;
regulation of biol. events using fusion proteins of
rapamycin-binding proteins and
rapamycin analogs)

IT Fas antigen

Transcription factors

RL: BPR (Biological process); BSU (Biological study, unclassified); BUU
(Biological use, unclassified); BIOL (Biological study); PROC (Process);
USES (Uses)

(fusion protein with FKBP12; regulation
of biol. events using fusion proteins of
rapamycin-binding proteins and
rapamycin analogs)

IT Molecular association

(of FKBP and rapamycin analogs; regulation of biol.
events using fusion proteins of rapamycin
-binding proteins and rapamycin analogs)

IT Protein motifs

(rapamycin binding; regulation of biol. events
using fusion proteins of rapamycin-
binding proteins and rapamycin analogs)

IT Apoptosis

(rapamycin induction of; regulation of biol. events using
fusion proteins of rapamycin-
binding proteins and rapamycin analogs)

IT Signal transduction, biological

Transcription, genetic

(rapamycin regulation of; regulation of biol. events using
fusion proteins of rapamycin-
binding proteins and rapamycin analogs)

IT Growth factor receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(rapamycin regulation of; regulation of biol. events using

fusion proteins of rapamycin-binding proteins and rapamycin analogs)

IT CD3 (antigen)
 RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
 (ζ chain, **fusion protein with FKBP12**
 ; regulation of biol. events using **fusion proteins of rapamycin-binding proteins and rapamycin analogs)**

IT 152406-15-0P 154074-71-2P 186757-74-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and reactions of, in preparation of fluoresceinated analog of **FK506**; regulation of biol. events using **fusion proteins of rapamycin-binding proteins and rapamycin analogs)**

IT 202522-62-1P
 RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation and reactions of; regulation of biol. events using **fusion proteins of rapamycin-binding proteins and rapamycin analogs)**

IT 104987-11-3, **FK506**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of fluoresceinated analog of; regulation of biol. events using **fusion proteins of rapamycin-binding proteins and rapamycin analogs)**

IT 186757-77-7P
 RL: ARU (Analytical role, unclassified); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation)
 (preparation of, fluoresceinated analog of **FK506**; regulation of biol. events using **fusion proteins of rapamycin-binding proteins and rapamycin analogs)**

IT 157054-81-4P 157054-82-5P 157054-84-7P
 157182-35-9P 157182-38-2P 157182-40-6P
 158472-50-5P 160349-48-4P 160401-32-1P
 161754-08-1P 161754-09-2P 167868-35-1P
 167868-36-2P 167938-80-9P 167938-82-1P
 186757-66-4P 186757-67-5P 186757-68-6P
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 232592-33-5P 232594-70-6P 232594-74-0P

RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation of; regulation of biol. events using **fusion proteins of rapamycin-binding proteins and rapamycin analogs**)

IT 12629-01-5, Human growth hormone

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(**rapamycin** regulation of expression of **gene** for, in transgenic mice; regulation of biol. events using **fusion proteins of rapamycin-binding proteins and rapamycin analogs**)

IT 155435-45-3P

RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(reactions of; regulation of biol. events using **fusion proteins of rapamycin-binding proteins and rapamycin analogs**)

IT 53123-88-9D, Rapamycin, analogs

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(regulation of biol. events using **fusion proteins of rapamycin-binding proteins and rapamycin analogs**)

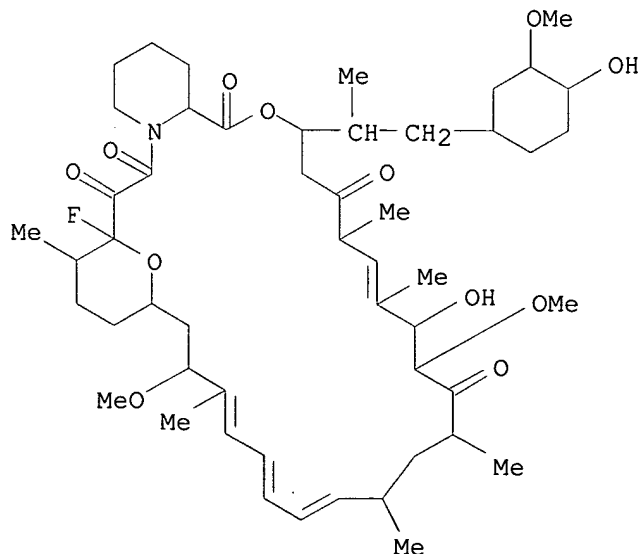
IT 202522-62-1P

RL: BUU (Biological use, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); USES (Uses)

(preparation and reactions of; regulation of biol. events using **fusion proteins of rapamycin-binding proteins and rapamycin analogs**)

RN 202522-62-1 HCAPLUS

CN Rapamycin, 14-deoxy-14-fluoro- (9CI) (CA INDEX NAME)



L82 ANSWER 4 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
 AN 1997:155088 HCAPLUS
 DN 126:153650
 ED Entered STN: 10 Mar 1997
 TI Regulation of biological processes using rapamycin and
 FK506-binding proteins fusion
 proteins
 IN Clackson, Timothy; Holt, Dennis A.; Gilman,
 Michael Z.
 PA Ariad Gene Therapeutics, Inc., USA; Clackson, Timothy; Holt,
 Dennis A.; Gilman, Michael Z.
 SO PCT Int. Appl., 49 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C12N0005-10
 ICS C12N0009-90; C12N0015-12; C12N0015-10; C12N0015-31; C12N0015-62;
 C12N0015-63; C12N0015-85; C12N0015-86; C07K0014-395; C07K0014-47;
 C07K0014-715; C12Q0001-68; A01K0067-027
 CC 3-1 (Biochemical Genetics)
 Section cross-reference(s): 6

FAN.CNT 4

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 9641865	A1	19961227	WO 1996-US9948	19960607 <--
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	US 2002107189	A1	20020808	US 2001-781804	20010212 <--
	US 6649595	B2	20031118		
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	US 1998-12097	A3	19980122		
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	US 2001-781804	A1	20010212		

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9641865	ICM	C12N0005-10
	ICS	C12N0009-90; C12N0015-12; C12N0015-10; C12N0015-31; C12N0015-62; C12N0015-63; C12N0015-85; C12N0015-86; C07K0014-395; C07K0014-47; C07K0014-715; C12Q0001-68; A01K0067-027
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C12N0015-62 [ICS,6]; C12N0015-63 [ICS,6]; C12N0015-85
[ICS,6]; C12N0015-86 [ICS,6]; C07K0014-395 [ICS,6];
C07K0014-47 [ICS,6]; C07K0014-715 [ICS,6]; C12Q0001-68
[ICS,6]; A01K0067-027 [ICS,6] <--
EP 833894 IPCI C12N0005-10 [ICM,6]; C12N0009-90 [ICS,6]; C12N0015-12
[ICS,6]; C12N0015-10 [ICS,6]; C12N0015-31 [ICS,6];
C12N0015-62 [ICS,6]; C12N0015-63 [ICS,6]; C12N0015-85
[ICS,6]; C12N0015-86 [ICS,6]; C07K0014-395 [ICS,6];
C07K0014-47 [ICS,6] <--
JP 2002514893 IPCI C12N0015-09 [ICM,7]; A01K0067-027 [ICS,7]; C12N0005-10
[ICS,7] <--
US 6187757 IPCI A61K0031-70; C12N0005-10
NCL 514/031.000; 435/325.000; 435/355.000; 435/372.000;
435/372.300; 435/375.000
US 2002107189 ECLA C07K014/715; C12N009/12B1; C12N015/10C6; C12N015/85 <--
IPCI A61K0038-17 [ICM,7]; C12P0021-02 [ICS,7]
NCL 514/012.000
ECLA C07D498/18+273D+311C+221C; C07K014/035; C07K014/395;
C07K014/47; C07K014/705B12; C07K014/705R; C07K014/715;
C12N009/12B1; C12N015/10C6; C12N015/85 <--
US 2003206891 IPCI A01K0067-027 [ICM,7]; A61K0048-00 [ICS,7];
A61K0031-4745 [ICS,7]; C12N0005-08 [ICS,7]
NCL 424/093.210
ECLA C07K014/715; C12N009/12B1; C12N015/10C6; C12N015/85 <--
US 2004082515 IPCI A61K0039-395 [ICM,7]; G01N0033-53 [ICS,7]
NCL 514/012.000
ECLA C07D498/18+273D+311C+221C; C07K014/035; C07K014/395;
C07K014/47; C07K014/705B12; C07K014/705R; C07K014/715;
C12N009/12B1; C12N015/10C6; C12N015/85 <--
OS MARPAT 126:153650
AB A method using **rapamycin** to regulate **gene** expression
or other processes in animal systems is described. The method uses
fusion proteins of an **FK506-binding**
protein (FKBP) and the **DNA-binding**
domain of a transcription factor, and of a **protein** capable of
binding to **FKBP:rapamycin** complexes such as
FRAP, Tor1, Tor2 with an activation domain. **Rapamycin** and the
FKBP and **FKBP:rapamycin-binding**
protein form a bridge that brings the **DNA-**
binding and activation domains together to form an active
transcription factor in the presence of **rapamycin**. The method
can be generally applied to any process regulated by **proteins**
with a similar domain structure.
ST **rapamycin gene** expression regulation; FRAP
fusion protein gene expression regulation;
FKBP12 fusion protein gene
expression regulation; **FKBP fusion protein**
gene expression regulation

- IT **Proteins, specific or class**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (FKBP (FK 506-binding protein), fusion products; regulation of biol. processes using rapamycin and FK506-binding proteins fusion proteins)
- IT **Proteins, specific or class**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (FKBP-12 (FK 506-binding protein, 12,000-mol.-weight), analogs, fusion products; regulation of biol. processes using rapamycin and FK506-binding proteins fusion proteins)
- IT **Proteins, specific or class**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (FRAP (FKBP-rapamycin-associated protein), fusion products; regulation of biol. processes using rapamycin and FK506-binding proteins fusion proteins)
- IT Transcription factors
 RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
 (GAL4, fusion products with FKBP12 and FRAP, regulation of gene expression by; regulation of biol. processes using rapamycin and FK506-binding proteins fusion proteins)
- IT **Genetic element**
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (IRES (internal ribosomal entry site) element, in bicistronic expression vectors; regulation of biol. processes using rapamycin and FK506-binding proteins fusion proteins)
- IT Transcription factors
 RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
 (NF-κB (nuclear factor κB), p65 subunit fusion products with FKBP12 and FRAP, regulation of gene expression by; regulation of biol. processes using rapamycin and FK506-binding proteins fusion proteins)
- IT Transcription factors
 RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
 (VP16, fusion products with FKBP12 and FRAP, regulation of gene expression by; regulation of biol. processes using rapamycin and FK506-binding proteins fusion proteins)
- IT **RNA formation factors**
 RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process);

- USES (Uses)
 (ZFHD1, **fusion** products with **FKBP12** and FRAP, regulation of **gene** expression by; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT **Gene**
 (**expression**, regulation by **rapamycin** of; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT **Chimeric gene**
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (for transcription factor **fusion** products with **FKBP12** and FRAP; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT **Fas antigen**
 RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
 (**fusion** products with **FKBP12** and FRAP, regulation of **gene** expression by; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT **Transcription factors**
 RL: BPR (Biological process); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); PROC (Process); USES (Uses)
 (**fusion** products, in **rapamycin** regulation of **gene** expression; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT **Proteins, specific or class**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (**gene TOR1, fusion products**; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT **Proteins, specific or class**
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (**gene TOR2, fusion products**; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT **Transcription factors**
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (**gene lexA, fusion products with rapamycin-binding proteins**, regulation of **DNA binding** by; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT **Promoter (genetic element)**
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (**interleukin 2, rapamycin** regulation of **gene** expression from; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)

- IT **Peptide library**
(of **fusion proteins** containing modified **FKBP** domains; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT **Plasmid vectors**
(p19BL87G6FKBP, chimeric gene for LexA-FKBP fusion protein, rapamycin regulation of DNA binding in relation to; regulation of biol. processes using rapamycin and FK506-binding proteins fusion proteins)
- IT **Plasmid vectors**
(p19BL87G6FRB, chimeric gene for LexA-FRB fusion protein, rapamycin regulation of DNA binding in relation to; regulation of biol. processes using rapamycin and FK506-binding proteins fusion proteins)
- IT **Tumor necrosis factor receptors**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(p55, fusion products with rapamycin-binding proteins; regulation of biol. processes using rapamycin and FK506-binding proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNN-1FRAPE-ZFHD1, ZFHD1-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and FK506-binding proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNN-1FRAPE-p65(361-550), FRAP-NF- κ B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and FK506-binding proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNN-1FRAPE-p65(450-550), FRAP-NF- κ B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and FK506-binding proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNN-1FRB-VP16, VP16-FRAP fusion protein gene on; regulation of biol. processes using rapamycin and FK506-binding proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNN-1FRB-p65(361-550), FRAP-NF- κ B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and FK506-binding proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNN-1FRB-p65(361-550)-IRES-ZFD1-3FKBP, chimeric genes for FRAP-NF- κ B p65 subunit and ZFD1-FKBP fusion proteins on; regulation of biol. processes using rapamycin and FK506-binding proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNN-1FRB-p65(450-550), FRAP-NF- κ B p65 subunit fusion protein gene on; regulation of biol. processes using rapamycin and FK506-binding proteins fusion proteins)

- IT **Plasmid vectors**
(pCGNN-2FRApe-ZFHD1, ZFHD1-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-2FRB-VP16, VP16-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-2FRB-p65(450-550), FRAP-NF- κ B p65 subunit fusion
protein gene on; regulation of biol. processes using
rapamycin and FK506-binding
proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNN-3FRApe-p65(361-550), FRAP-NF- κ B p65 subunit fusion
protein gene on; regulation of biol. processes using
rapamycin and FK506-binding
proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNN-3FRApe-p65(450-550), FRAP-NF- κ B p65 subunit fusion
protein gene on; regulation of biol. processes using
rapamycin and FK506-binding
proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNN-3FRB, gene for FLAG-labeled FRB on;
regulation of biol. processes using rapamycin and
FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-FRAPb-p65, FRAP-NF- κ B p65 subunit fusion
protein gene on; regulation of biol. processes using
rapamycin and FK506-binding
proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNN-FRAPc-p65, FRAP-NF- κ B p65 subunit fusion
protein gene on; regulation of biol. processes using
rapamycin and FK506-binding
proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNN-FRAPd-p65, FRAP-NF- κ B p65 subunit fusion
protein gene on; regulation of biol. processes using
rapamycin and FK506-binding
proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNN-FRApe-p65, FRAP-NF- κ B p65 subunit fusion
protein gene on; regulation of biol. processes using
rapamycin and FK506-binding
proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNN-FRAPa-p65, FRAP-NF- κ B p65 subunit fusion
protein gene on; regulation of biol. processes using
rapamycin and FK506-binding
proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNN-GAL-2FRB, GAL4-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)

- IT **Plasmid vectors**
(pCGNN-GAL-3FRB, GAL4-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-GAL-4FRB, GAL4-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-GAL-FRAPb, GAL4-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-GAL-FRAPc, GAL4-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-GAL-FRAPd, GAL4-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-GAL-FRAPe, GAL4-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-GAL-FRAPf, GAL4-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-GAL-FRAPg, GAL4-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-GAL-FRAPh, GAL4-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-GAL-FRAPi, GAL4-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-GAL-FRAPa, GAL4-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-ZFHD1-1FRB, ZFHD1-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)

- IT **Plasmid vectors**
(pCGNN-ZFHD1-2FRAPe, ZFHD1-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-ZFHD1-2FRB, ZFHD1-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-ZFHD1-3FRAPe, ZFHD1-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-ZFHD1-4FRAPe, ZFHD1-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-ZFHD1-FRAPb, ZFHD1-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-ZFHD1-FRAPe, ZFHD1-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-ZFHD1-FRAPa, ZFHD1-FRAP fusion protein
gene on; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Plasmid vectors**
(pCGNN-p65(361-550)-1FRAPe, FRAP-NF- κ B p65 subunit fusion
protein gene on; regulation of biol. processes using
rapamycin and FK506-binding
proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNN-p65(361-550)-3FRAPe, FRAP-NF- κ B p65 subunit fusion
protein gene on; regulation of biol. processes using
rapamycin and FK506-binding
proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNN-p65(450-550)-1FRAPe, FRAP-NF- κ B p65 subunit fusion
protein gene on; regulation of biol. processes using
rapamycin and FK506-binding
proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNN-p65(450-550)-3FRAPe, FRAP-NF- κ B p65 subunit fusion
protein gene on; regulation of biol. processes using
rapamycin and FK506-binding
proteins fusion proteins)
- IT **Plasmid vectors**
(pCGNNZFHD1-FKBPx1, ZFHD1-FKBP12 fusion
protein gene on; regulation of biol. processes using
rapamycin and FK506-binding
proteins fusion proteins)

- IT **Plasmid vectors**
(pCGNNZFHD1-FKBPx3, ZFHD1-FKBP12 fusion
protein gene on; regulation of biol. processes using
rapamycin and FK506-binding
proteins fusion proteins)
- IT **Plasmid vectors**
(pZHWTx12-CMV-SEAP, secreted alkaline phosphatase reporter gene
on, rapamycin regulation of expression of; regulation of
biol. processes using rapamycin and FK506-
binding proteins fusion proteins)
- IT **Plasmid vectors**
(pZHWTx12-CMV-hGH, human growth hormone reporter gene on,
rapamycin regulation of expression of; regulation of biol.
processes using rapamycin and FK506-binding
proteins fusion proteins)
- IT **Plasmid vectors**
(pZHWTx12-IL2-SEAP, secreted alkaline phosphatase reporter gene
on, rapamycin regulation of expression from IL2 promoter of;
regulation of biol. processes using rapamycin and
FK506-binding proteins fusion
proteins)
- IT **Myristoylation**
(peptide target for, incorporation into FKBP of;
regulation of biol. processes using rapamycin and
FK506-binding proteins fusion
proteins)
- IT **Nerve growth factor receptors**
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU
(Biological use, unclassified); BIOL (Biological study); PROC (Process);
USES (Uses)
(p75, fusion products with FKBP and FRAP, in
rapamycin regulation of apoptosis; regulation of biol.
processes using rapamycin and FK506-binding
proteins fusion proteins)
- IT **Interleukin 2**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(rapamycin regulation of expression from promoter of
gene for; regulation of biol. processes using rapamycin
and FK506-binding proteins fusion
proteins)
- IT **Apoptosis**
Cell differentiation
Cell proliferation
Signal transduction, biological
Transcription, genetic
(regulation by rapamycin of; regulation of biol. processes
using rapamycin and FK506-binding
proteins fusion proteins)
- IT **CD3 (antigen)**
RL: BPR (Biological process); BSU (Biological study, unclassified); BUU
(Biological use, unclassified); BIOL (Biological study); PROC (Process);
USES (Uses)
(ζ -chain, fusion products with FKBP12 and
FRAP, regulation of gene expression by; regulation of biol.
processes using rapamycin and FK506-binding
proteins fusion proteins)
- IT **80449-02-1, Protein tyrosine kinase**
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL
(Biological study); PROC (Process)
(activation by rapamycin of; regulation of biol. processes

- using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT 186847-32-5 186847-34-7 186847-36-9
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (amino acid sequence; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT 162926-18-3
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (biotinylation of; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT 104987-11-3, **FK506**
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (conjugation with fluorescein of; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT 186845-13-6 186845-14-7
 RL: BUU (Biological use, unclassified); PRP (Properties); BIOL (Biological study); USES (Uses)
 (nucleotide sequence, **chimeric genes** containing; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT 186847-33-6 186847-35-8 186847-37-0
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (nucleotide sequence; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT 152406-15-0P 154074-71-2P 186757-74-4P 186757-77-7P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (preparation and reactions of, in preparation fluoresceinated **FK506**; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT 186757-82-4P
 RL: ARG (Analytical reagent use); SPN (Synthetic preparation); ANST (Analytical study); PREP (Preparation); USES (Uses)
 (preparation of; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT 186757-79-9P 186757-80-2P 186757-81-3P
 RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)
 (**rapamycin** analog, **binding** to FRAP of complexes with **FKBP**; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT 178446-27-0
 RL: BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (**rapamycin** analog, regulation of apoptosis using; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)
- IT 53123-88-9D, **Rapamycin**, analogs
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)

IT 161754-08-1P 161754-09-2P 186757-66-4P
186757-67-5P 186757-68-6P 186757-69-7P
186757-70-0P 186757-71-1P 186757-72-2P
186757-73-3P 186794-75-2P 186794-97-8P

RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)

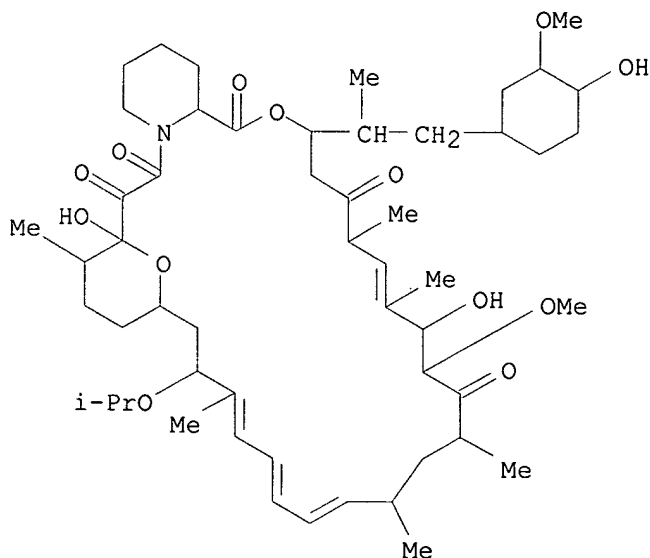
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RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation); PROC (Process)

(**rapamycin** analog, **binding** to FRAP of complexes with **FKBP**; regulation of biol. processes using **rapamycin** and **FK506-binding proteins fusion proteins**)

RN 186757-79-9 HCAPLUS

CN Rapamycin, 7-O-demethyl-7-O-(1-methylethyl)- (9CI) (CA INDEX NAME)



L82 ANSWER 5 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN

AN 1995:994704 HCAPLUS

DN 124:45690

ED Entered STN: 22 Dec 1995

TI Molecular cloning of **cDNA** for human effector **proteins** of **rapamycin**

IN Molnar-Kimber, Katherine Lu; Failli, Amedeo Arturo; Caggiano, Thomas Joseph; Nakanishi, Koji; Chen, Yanqiu

PA American Home Products Corp., USA; Trustees of Columbia University in the City of New York; Wyeth

SO Eur. Pat. Appl., 44 pp.

CODEN: EPXXDW

DT Patent
 LA English
 IC ICM C12N0015-12
 ICS C07K0014-705; G01N0033-68; A61K0031-70
 CC 1-6 (Pharmacology)
 Section cross-reference(s): 13

FAN.CNT 2

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	EP 676471	A2	19951011	EP 1995-301475	19950307 <--
	EP 676471	A3	19970820		
	EP 676471	B1	20040929		
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	IL 112873	A1	20050320	IL 1995-112873	19950303 <--
	HU 72189	A2	19960328	HU 1995-673	19950306 <--
	HU 218109	B	20000628		
	JP 08059696	A2	19960305	JP 1995-47408	19950307 <--
	AT 278015	E	20041015	AT 1995-301475	19950307 <--
	CA 2144223	AA	19950909	CA 1995-2144223	19950308 <--
	AU 9513670	A1	19950914	AU 1995-13670	19950308 <--
	ZA 9501931	A	19960909	ZA 1995-1931	19950308 <--
	TW 404951	B	20000911	TW 1995-84102190	19950506 <--
	AU 9917390	A1	19990520	AU 1999-17390	19990219 <--
	AU 775722	B2	20040812	AU 2001-78263	20011008 <--
PRAI	US 1994-207975	A	19940308	<--	
	US 1994-312023	A	19940926	<--	
	US 1995-384524	A	19950213	<--	
	AU 1995-13670	A3	19950308	<--	
	AU 1999-17390	A3	19990219		

CLASS

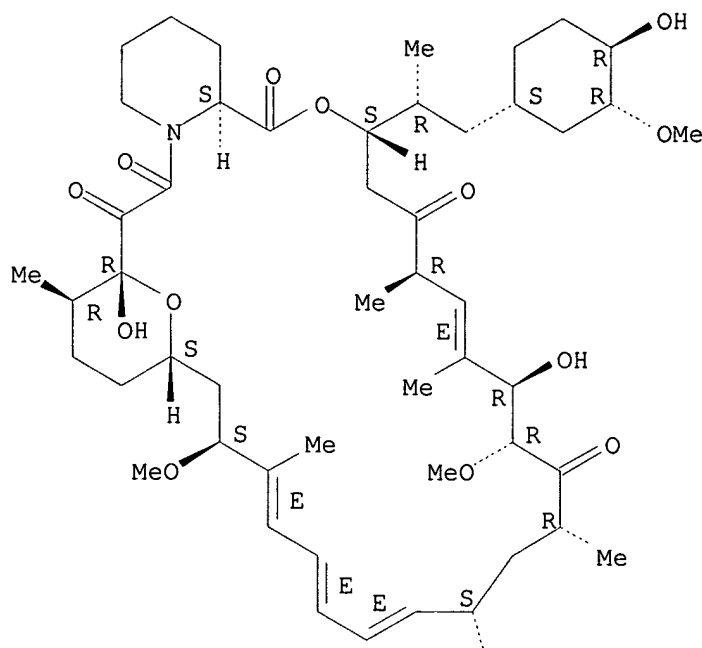
PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
EP 676471	ICM	C12N0015-12
	ICS	C07K0014-705; G01N0033-68; A61K0031-70
	IPCI	C12N0015-12 [ICM,6]; C07K0014-705 [ICS,6]; G01N0033-68 [ICS,6]; A61K0031-70 [ICS,6]
	ECLA	C07K014/705; C12N009/12B1; G01N033/68 <--
IL 112873	IPCI	C12N0015-12 [ICM,7]; C07K0014-705 [ICS,7]; G01N0033-68 [ICS,7] <--
HU 72189	IPCI	C07K0014-435 [ICM,6]; C07K0001-22 [ICS,6]; C07H0021-00 [ICS,6]; C12N0015-09 [ICS,6] <--
JP 08059696	IPCI	C07K0014-47 [ICM,6]; A61K0031-70 [ICS,6]; A61K0048-00 [ICS,6]; C07H0021-04 [ICS,6]; C12N0015-09 [ICS,6]; C12P0021-02 [ICS,6]; G01N0033-53 [ICS,6]; C12P0021-02 [ICI,6]; C12R0001-19 [ICI,6] <--
AT 278015	IPCI	C12N0015-12 [ICM,7]; C07K0014-705 [ICS,7]; G01N0033-68 [ICS,7]; A61K0031-70 [ICS,7] <--
CA 2144223	IPCI	C12N0015-12 [ICM,6]; C07K0014-705 [ICS,6]; C07H0021-00 [ICS,6]; A61K0048-00 [ICS,6]; A61K0031-70 [ICS,6]; G01N0033-566 [ICS,6] <--
AU 9513670	IPCI	C07K0014-725 [ICM,6]; C07K0014-705 [ICS,6]; C07K0014-47 [ICS,6]; C12N0015-31 [ICS,6]; C12N0015-11 [ICS,6]; G01N0033-68 [ICS,6]; A61K0038-00 [ICS,6] <--
ZA 9501931	IPCI	C12N [ICM,6]; C07K [ICS,6]; G01N [ICS,6]; A61K [ICS,6] <--
TW 404951	IPCI	C07K0014-47 [ICM,7]; C12N0015-12 [ICS,7]; G01N0033-68 [ICS,7] <--
AU 9917390	IPCI	C07K0014-47 [ICM,6]; C07H0021-02 [ICS,6]; C07H0021-04 [ICS,6]; A61K0038-17 [ICS,6]; G01N0033-68 [ICS,6] <--
AU 775722	IPCI	C07K0014-47 [ICM,7]; A61K0038-17 [ICS,7]; C07H0021-02

- [ICS,7]; C07H0021-04 [ICS,7]; C12N0015-12 [ICS,7] <--
- AB Novel **rapamycin** effector **proteins** having mol. weight (SDS-PAGE) 210 kDa, 208 kDa, 148 kDa, and 125 kDa, resp., are identified from human leukemia cell line Molt 4 using a **fusion protein** of glutathione S-transferase-FK506 **binding protein** 12 (GST-FKBP) produced by *Escherichia coli* transformed with plasmid pGEX-FKBP. The 210-kDa **protein** is further isolated using the GST-FKBP12-**rapamycin** complex from BJAB cells and normal human T cells. The **cDNA** for 210-kDa **protein** is isolated and its amino acid sequence determined. Therapeutic uses of the **proteins** as immunomodulatory agents, anti-restenosis or anti-tumor agents are claimed. Also claimed are the antisense **RNA** and antisense **DNA** of the **cDNA**.
- ST **cDNA** human **rapamycin** effector **protein** sequence
- IT **Gene**, animal
RL: BSU (Biological study, unclassified); NUU (Other use, unclassified); BIOL (Biological study); USES (Uses)
(cloning of **cDNA** for 210-kDa human effector **protein** of **rapamycin**)
- IT **Protein sequences**
(of 210-kDa human effector **protein** of **rapamycin**)
- IT Immunomodulators
Neoplasm inhibitors
(**recombinant** human effector **proteins** of **rapamycin** as)
- IT **Ribonucleic acids**
RL: BSU (Biological study, unclassified); NUU (Other use, unclassified); BIOL (Biological study); USES (Uses)
(**antisense**, of **cDNA** for 210-kDa human effector **protein** of **rapamycin**)
- IT **Deoxyribonucleic acid sequences**
(complementary, for 210-kDa human effector **protein** of **rapamycin**)
- IT **Deoxyribonucleic acids**
RL: BSU (Biological study, unclassified); NUU (Other use, unclassified); BIOL (Biological study); USES (Uses)
(**complementary, antisense**, of **cDNA** for 210-kDa human effector **protein** of **rapamycin**)
- IT Heart, disease
(restenosis, **recombinant** human effector **proteins** of **rapamycin** for treatment of)
- IT 171341-72-3
RL: PRP (Properties)
(amino acid sequence; cloning of **cDNA** for human effector **proteins** of **rapamycin**)
- IT 171341-74-5
RL: NUU (Other use, unclassified); PRP (Properties); USES (Uses)
(amino acid sequence; for isolation human effector **proteins** of **rapamycin**)
- IT 171728-91-9 171728-92-0 171728-93-1 171728-94-2
RL: PRP (Properties)
(amino acid sequence; fragment of 210-kDa **rapamycin** effector **protein** binding to glutathione S-transferase-FK506 **binding protein-rapamycin** complex (RAPA-GST-FKBP))
- IT 53123-88-9, **Rapamycin**
RL: MSC (Miscellaneous)
(cloning of **cDNA** for human effector **proteins** of

rapamycin)
IT 50812-37-8, Glutathione S-transferase
RL: BSU (Biological study, unclassified); NUU (Other use, unclassified);
BIOL (Biological study); USES (Uses)
(**fusion** products with **FK506**; isolation of human
effector **proteins** of **rapamycin** using)
IT 104987-11-3D, **FK506**, **fusion** products with glutathione
S-transferase
RL: BSU (Biological study, unclassified); NUU (Other use, unclassified);
BIOL (Biological study); USES (Uses)
(isolation of human effector **proteins** of **rapamycin**
using)
IT 171341-71-2
RL: PRP (Properties)
(nucleotide sequence; cloning of **cDNA** for human effector
proteins of **rapamycin**)
IT 171341-73-4
RL: NUU (Other use, unclassified); PRP (Properties); USES (Uses)
(nucleotide sequence; for isolation human effector **proteins**
of **rapamycin**)
IT 143030-02-8 143135-97-1 143136-00-9
143136-08-7 151477-92-8 171728-96-4
RL: NUU (Other use, unclassified); USES (Uses)
(**rapamycin** analog; for isolation of human 210-kDa
rapamycin effector **protein binding** to
glutathione S-transferase-**FK506 binding**
protein-rapamycin complex (RAPA-GST-**FKBP**))
IT 53123-88-9, **Rapamycin**
RL: MSC (Miscellaneous)
(cloning of **cDNA** for human effector **proteins** of
rapamycin)
RN 53123-88-9 HCAPLUS
CN Rapamycin (9CI) (CA INDEX NAME)

Absolute stereochemistry.
Double bond geometry as shown.

PAGE 1-A



PAGE 2-A

Me

L82 ANSWER 6 OF 6 HCAPLUS COPYRIGHT 2006 ACS on STN
 AN 1994:212008 HCAPLUS
 DN 120:212008
 ED Entered STN: 30 Apr 1994
 TI Methods and reagents for the determination of immunosuppressive agents and their **binding proteins**
 IN Lane, Benjamin Clay; Luly, Jay Richard; Smith, Allan H.; Bolling, Timothy J.; Mandecki, Wldozimierz; Pilot-Matias, Tami J.
 PA Abbott Laboratories, USA
 SO PCT Int. Appl., 53 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C07D0221-18
 ICS C07D0221-22; C07K0003-00; C07K0013-00; C07K0015-00; C07K0017-00; C12Q0001-00; G01N0033-53
 CC **9-2 (Biochemical Methods)**
 Section cross-reference(s): 1, 3, 15, 26
 FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9325533	A1	19931223	WO 1993-US5197	19930601 <--
W: AU, CA, JP, KR				

RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
 AU 9344005 A1 19940104 AU 1993-44005 19930601 <--
 PRAI US 1992-893858 A 19920605 <--
 WO 1993-US5197 A 19930601 <--

CLASS

PATENT NO.	CLASS	PATENT FAMILY CLASSIFICATION CODES
WO 9325533	ICM	C07D0221-18
	ICS	C07D0221-22; C07K0003-00; C07K0013-00; C07K0015-00; C07K0017-00; C12Q0001-00; G01N0033-53
	IPCI	C07D0221-18 [ICM,5]; C07D0221-22 [ICS,5]; C07K0003-00 [ICS,5]; C07K0013-00 [ICS,5]; C07K0015-00 [ICS,5]; C07K0017-00 [ICS,5]; C12Q0001-00 [ICS,5]; G01N0033-53 [ICS,5] <--
AU 9344005	IPCI	C12Q0001-00 [ICM,5]; G01N0033-53 [ICS,5]; C07D0221-18 [ICS,5]; C07D0221-22 [ICS,5]; C07K0003-00 [ICS,5]; C07K0013-00 [ICS,5]; C07K0015-00 [ICS,5]; C07K0017-00 [ICS,5] <--

OS MARPAT 120:212008

AB Assay methods and reagents for determining the presence or amount of immunophilin

ligands and immunophilins thereof employing a **recombinant fusion protein** comprising (i) an immunosuppressant **binding protein** and (ii) a heterologous **protein** are disclosed. The **recombinant fusion protein** can also be employed for the evaluation of immunosuppressive activities of immunosuppressive agents in order to determine their efficacy during the course of therapeutic treatment of a patient. Preferably, the **recombinant fusion protein** comprises a macrolide immunosuppressive agent and CTP:CMP-3-deoxy-D-manno-octulosonate cytidyl transferase (CKS). When employed in a **binding** assay format, the **recombinant fusion protein** provides higher reactivity for the immunophilin ligand under determination than does the native immunosuppressant **binding protein**. Also provided are ascomycin (or **FK-506**) and **rapamycin** analog conjugates with macromols. or detectable moieties. In particular, an immunosuppressant assay reagent comprising **recombinantly-prepared human FK-506 binding protein (FKBP)-CKS fusion protein** immobilized on a solid support material provides a higher signal-to-noise ratio when employed in a competitive heterogeneous assay format than when native **FKBP** immobilized on a solid support material is employed in such assay format. Ascomycin-C22-carboxymethyloxime-alkaline phosphatase conjugate was also prepared and used as a reagent in assays.

ST immunosuppressant assay **fusion protein** reagent;
chimeric binding protein immunosuppressant reagent;
 immunophilin **fusion protein** immunosuppressant assay;
FK 506 binding protein fusion reagent;
 CMP KDO synthetase **fusion protein**;
 ascomycin alk phosphatase conjugate reagent

IT Immunoglobulins

RL: ANST (Analytical study)
 (Fc fragment, **fusion** products with immunosuppressant-
binding protein, for reagent for determination of
 immunosuppressant or **binding protein**)

IT Blood analysis

(ascomycin determination in, immobilized **FK-506-binding protein**-CMP-KDO synthetase as reagent in)

IT **Proteins, specific or class**

- RL: ANST (Analytical study)
(**ascomycin-binding**, determination of, immunosuppressant-
binding protein-heterologous protein
fusion product as reagent for)
- IT **Gene**, animal
RL: SPN (Synthetic preparation); PREP (Preparation)
(**cDNA**, for **FK-506-binding**
protein of human, in **recombinant** preparation of
fusion protein with CMP-KDO synthetase for
immunosuppressant assay)
- IT Chromophores and Chromophoric systems
Fluorescent substances
Luminescent substances
Phosphorescent substances
Enzymes
Macromolecular compounds
RL: ANST (Analytical study)
(conjugates with ascomycin or **rapamycin** analogs, for determination of
immunosuppressant or its **binding protein**)
- IT **Proteins, specific or class**
RL: ANST (Analytical study)
(**cyclosporin-binding**, determination of, immunosuppressant-
binding protein-heterologous protein
fusion product as reagent for)
- IT Immunosuppressants
(determination of, immunosuppressant-**binding protein**
-heterologous **protein fusion** product as reagent
for)
- IT Ligands
RL: ANST (Analytical study)
(for immunophilin, determination of, immunosuppressant-**binding**
protein-heterologous protein fusion product
as reagent for)
- IT **Proteins, specific or class**
RL: ANST (Analytical study)
(immunosuppressant-**binding**, determination of, immunosuppressant-
binding protein-heterologous protein
fusion product as reagent for)
- IT Calmodulins
RL: ANST (Analytical study)
(phosphatase activated by calcium or, immunophilin or immunophilin
ligand labeled with, for reagent)
- IT **Proteins, specific or class**
RL: ANST (Analytical study)
(**rapamycin-binding**, determination of, immunosuppressant-
binding protein-heterologous protein
fusion product as reagent for)
- IT Antibodies
RL: SPN (Synthetic preparation); PREP (Preparation)
(to ascomycin-keyhole limpet hemocyanin, preparation of, for
immunosuppressant assay reagent)
- IT **Proteins, specific or class**
RL: ANT (Analyte); ANST (Analytical study)
(**FKBP (FK 506-binding**
protein), determination of, immunosuppressant-**binding**
protein-heterologous protein fusion product
as reagent for)
- IT Luminescent substances
(chemi-, conjugates with ascomycin or **rapamycin** analogs, for
determination of immunosuppressant or its **binding protein**)

- IT **Gene**
 RL: PROC (Process)
 (chimeric, for **FK-506-binding protein-CMP-KDO synthetase fusion product**,
expression of, immunosuppressant assay in relation to)
- IT Albumins, compounds
 Hemocyanins
 Thyroglobulins
 RL: ANST (Analytical study)
 (conjugates, with ascomycin or **rapamycin** analogs, for determination
 of immunosuppressant or its **binding protein**)
- IT **Proteins, specific or class**
 RL: ANST (Analytical study)
 (fusion products, of immunosuppressant-
binding protein and heterologous **protein**,
 for reagent for determination of immunosuppressant or **binding**
protein)
- IT **Proteins, specific or class**
 RL: ANT (Analyte); ANST (Analytical study)
 (immunophilins, determination of, immunosuppressant-**binding**
protein-heterologous protein fusion product
 as reagent for)
- IT 9013-05-2, Phosphatase
 RL: ANST (Analytical study)
 (calcium/calmodulin-activated, immunophilin or immunophilin ligand
 labeled with, for reagent)
- IT 9025-75-6, Calcineurin
 RL: ANT (Analyte); ANST (Analytical study)
 (determination of, immobilized **FK-506-binding**
protein-CMP-KDO synthetase as reagent in)
- IT **53123-88-9, Rapamycin** 79217-60-0, Cyclosporin
 104987-11-3, **FK-506** 104987-12-4, Ascomycin
 RL: ANT (Analyte); ANST (Analytical study)
 (determination of, immunosuppressant-**binding protein**
 -heterologous **protein fusion product** as reagent
 for)
- IT **53123-88-9D, Rapamycin**, analogs, conjugates with
 macromol. or detectable moiety 104987-12-4D, Ascomycin, analogs,
 conjugates with macromol. or detectable moiety
 RL: ANST (Analytical study)
 (for immunosuppressant or its **binding protein** determination
 using immunosuppressant-**binding protein**
 -heterologous **protein fusion product**)
- IT 37278-28-7D, CMP-KDO synthetase, **fusion products** with
 immunosuppressant-**binding protein** 50812-37-8D,
 Glutathione S-transferase, **fusion products** with
 immunosuppressant-**binding protein**
 RL: ANST (Analytical study)
 (for reagent for determination of immunosuppressant or **binding**
protein)
- IT 9001-78-9D, Alkaline phosphatase, conjugates with ascomycin or
rapamycin analogs
 RL: ANST (Analytical study)
 (immunosuppressant or its **binding protein** determination
 using immunosuppressant-**binding protein**
 -heterologous **protein fusion product** and, as
 reagents)
- IT 7440-70-2, Calcium, biological studies
 RL: BIOL (Biological study)
 (phosphatase activated by calmodulin or, immunophilin or immunophilin

ligand labeled with, for reagent)

IT 104987-30-6P **153984-91-9P**
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
 (Reactant or reagent)
 (preparation and reaction of, in preparation of reagent for
 immunosuppressant
 assay)

IT 148146-86-5DP, conjugates with alkaline phosphatase and other **proteins**
 153984-92-0P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (preparation of, for reagent for immunosuppressant assay)

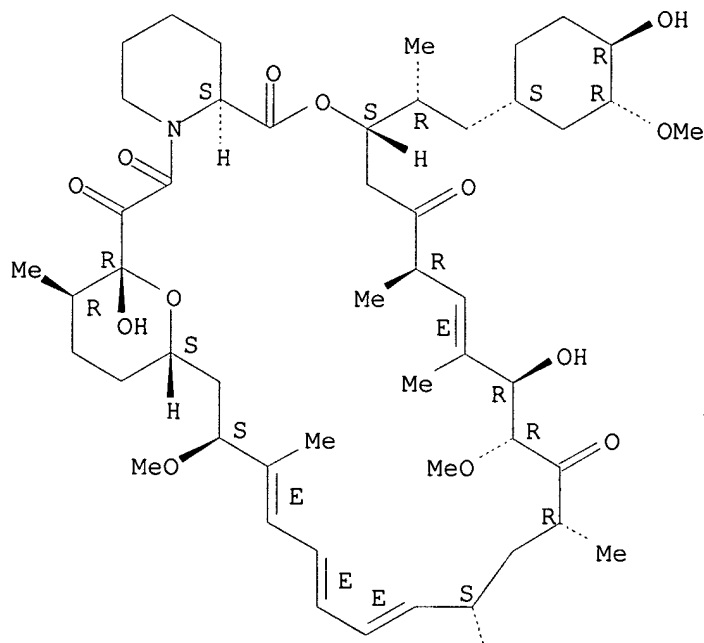
IT 2921-14-4, Carboxymethoxylamine hemihydrochloride
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (reaction of, with ascomycin, in preparation of reagent for
 immunosuppressant assay)

IT **53123-88-9, Rapamycin**
 RL: ANT (Analyte); ANST (Analytical study)
 (determination of, immunosuppressant-**binding protein**
 -heterologous **protein fusion** product as reagent
 for)

RN 53123-88-9 HCAPLUS
 CN Rapamycin (9CI) (CA INDEX NAME)

Absolute stereochemistry.
 Double bond geometry as shown.

PAGE 1-A



PAGE 2-A

Me

=> fil reg

FILE 'REGISTRY' ENTERED AT 07:22:43 ON 09 FEB 2006

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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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STRUCTURE FILE UPDATES: 7 FEB 2006 HIGHEST RN 873775-18-9

DICTIONARY FILE UPDATES: 7 FEB 2006 HIGHEST RN 873775-18-9

New CAS Information Use Policies, enter HELP USAGETERMS for details.

TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

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*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Structure search iteration limits have been increased. See HELP SLIMITS for details.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=> => d l83 ide can 1 10 20 30 40 50 60 70 80 90 100 110 120 130 140 150 160 166

L83 ANSWER 1 OF 166 REGISTRY COPYRIGHT 2006 ACS on STN

RN 328060-38-4 REGISTRY

ED Entered STN: 20 Mar 2001

CN Rapamycin, 7-demethoxy-7-[[[(dimethylamino)oxy]methyl]oxy]methyl]-(7R,31S)-(9CI) (CA INDEX NAME)

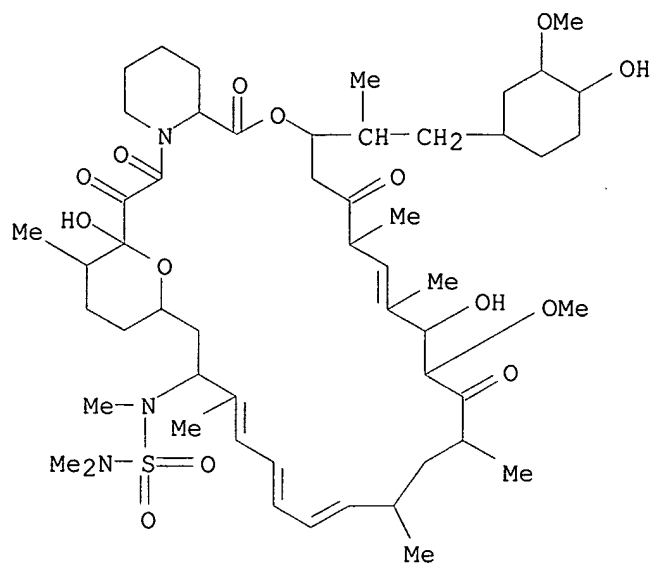
FS STEREOSEARCH

MF C53 H85 N3 O14 S

SR CA

LC STN Files: CA, CAPLUS

Sample
lists



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:193290

L83 ANSWER 10 OF 166 REGISTRY COPYRIGHT 2006 ACS on STN

RN **328060-29-3** REGISTRY

ED Entered STN: 20 Mar 2001

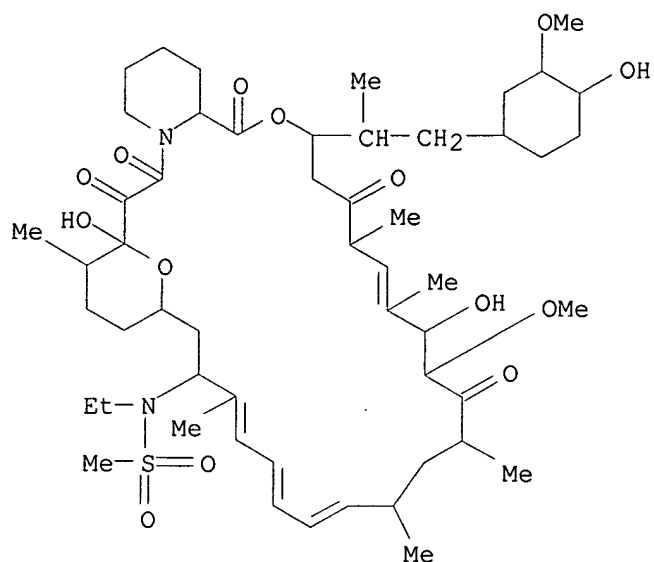
CN Rapamycin, 7-demethoxy-7-[ethyl(methylsulfonyl)amino]-, (7R,31S)- (9CI)
(CA INDEX NAME)

FS STEREOSEARCH

MF C53 H84 N2 O14 S

SR CA

LC STN Files: CA, CAPLUS

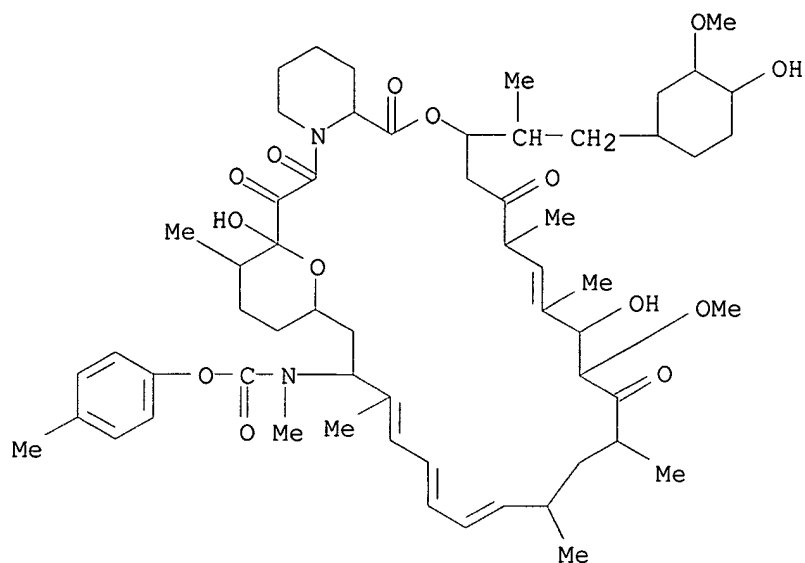


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

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1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:193290

L83 ANSWER 20 OF 166 REGISTRY COPYRIGHT 2006 ACS on STN
RN **328060-19-1** REGISTRY
ED Entered STN: 20 Mar 2001
CN Rapamycin, 7-demethoxy-7-[methyl[(4-methylphenoxy)carbonyl]amino]-, (31S)-
(9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C59 H86 N2 O14
SR CA
LC STN Files: CA, CAPLUS

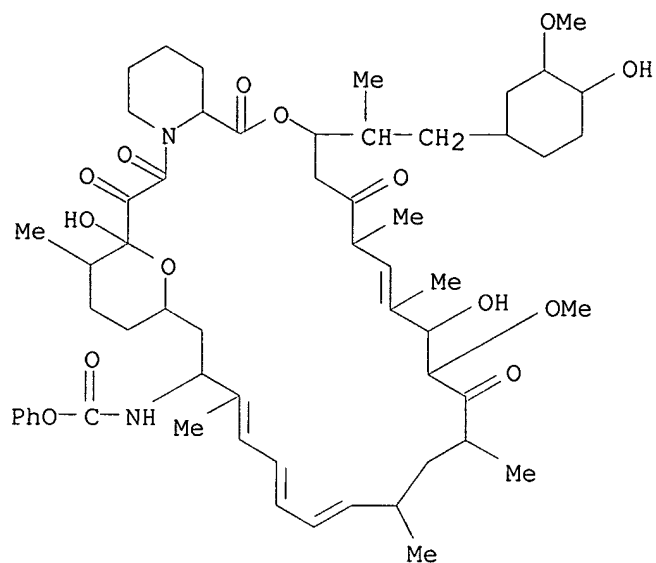


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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:193290

L83 ANSWER 30 OF 166 REGISTRY COPYRIGHT 2006 ACS on STN
RN **328060-09-9** REGISTRY
ED Entered STN: 20 Mar 2001
CN Rapamycin, 7-demethoxy-7-[(phenoxy-carbonyl)amino]-, (31S)- (9CI) (CA
INDEX NAME)
FS STEREOSEARCH
MF C57 H82 N2 O14
SR CA
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:193290

L83 ANSWER 40 OF 166 REGISTRY COPYRIGHT 2006 ACS on STN

RN **328059-99-0** REGISTRY

ED Entered STN: 20 Mar 2001

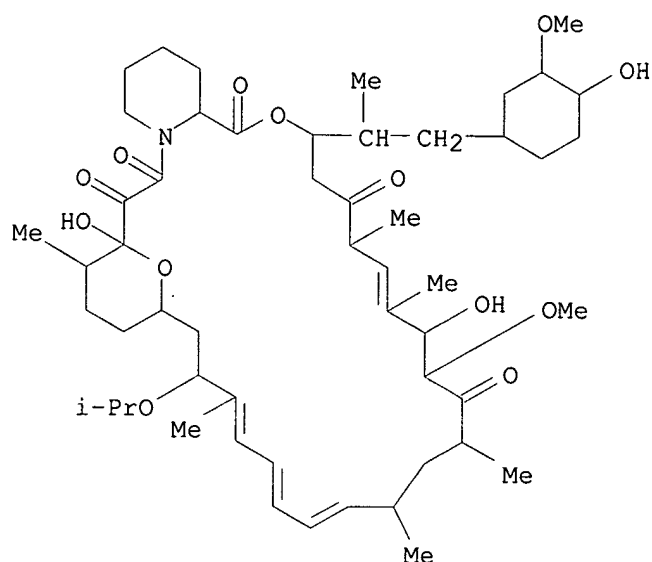
CN Rapamycin, 7-O-demethyl-7-O-(1-methylethyl)-, (7R,31S)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C53 H83 N O13

SR CA

LC STN Files: CA, CAPLUS

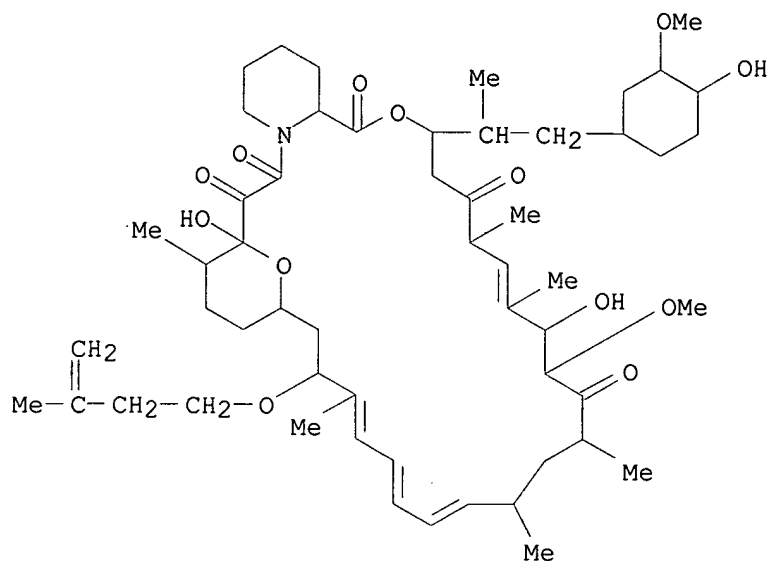


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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:193290

L83 ANSWER 50 OF 166 REGISTRY COPYRIGHT 2006 ACS on STN
RN **328059-89-8** REGISTRY
ED Entered STN: 20 Mar 2001
CN Rapamycin, 7-O-demethyl-7-O-(3-methyl-3-butenyl)-, (31S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C55 H85 N O13
SR CA
LC STN Files: CA, CAPLUS

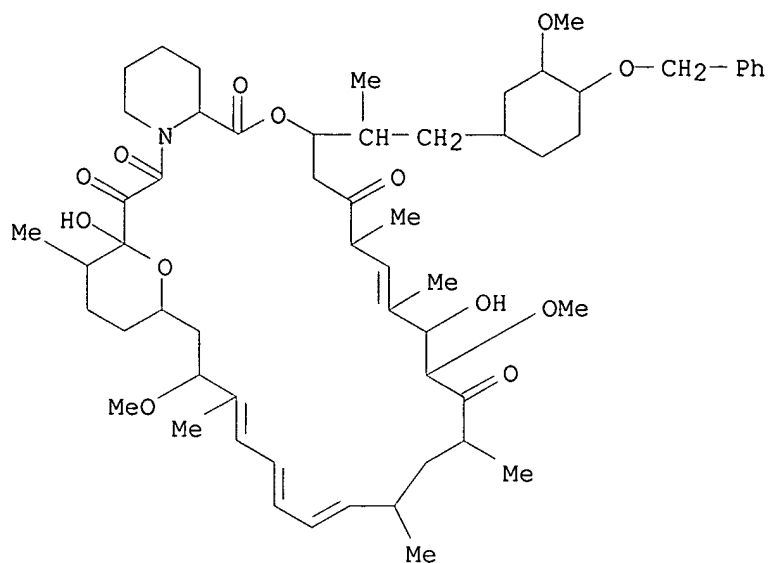


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:193290

L83 ANSWER 60 OF 166 REGISTRY COPYRIGHT 2006 ACS on STN
RN **328059-79-6** REGISTRY
ED Entered STN: 20 Mar 2001
CN Rapamycin, 42-O-(phenylmethyl)-, (31S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C58 H85 N O13
SR CA
LC STN Files: CA, CAPLUS

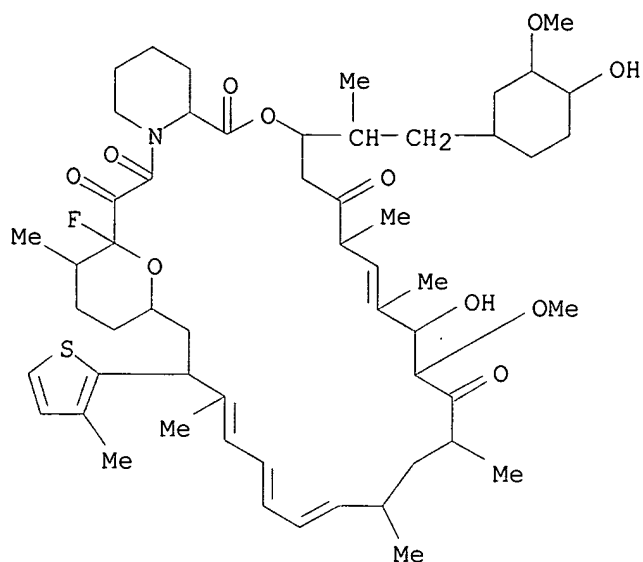


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:193290

L83 ANSWER 70 OF 166 REGISTRY COPYRIGHT 2006 ACS on STN
RN **232594-70-6** REGISTRY
ED Entered STN: 13 Aug 1999
CN Rapamycin, 7-demethoxy-14-deoxy-14-fluoro-7-(3-methyl-2-thienyl)- (9CI)
(CA INDEX NAME)
FS STEREOSEARCH
MF C55 H80 F N O11 S
SR CA
LC STN Files: CA, CAPLUS

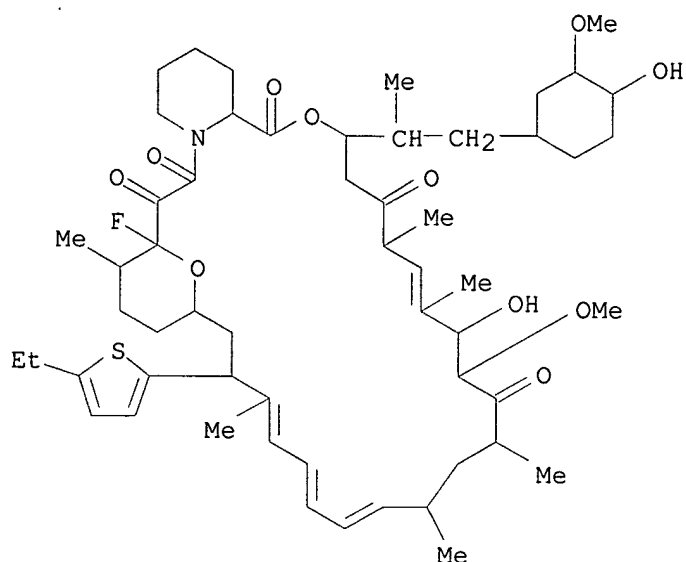


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1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:112371

L83 ANSWER 80 OF 166 REGISTRY COPYRIGHT 2006 ACS on STN
RN **232592-23-3** REGISTRY
ED Entered STN: 13 Aug 1999
CN Rapamycin, 7-demethoxy-14-deoxy-7-(5-ethyl-2-thienyl)-14-fluoro- (9CI)
(CA INDEX NAME)
FS STEREOSEARCH
MF C56 H82 F N O11 S
SR CA
LC STN Files: CA, CAPLUS

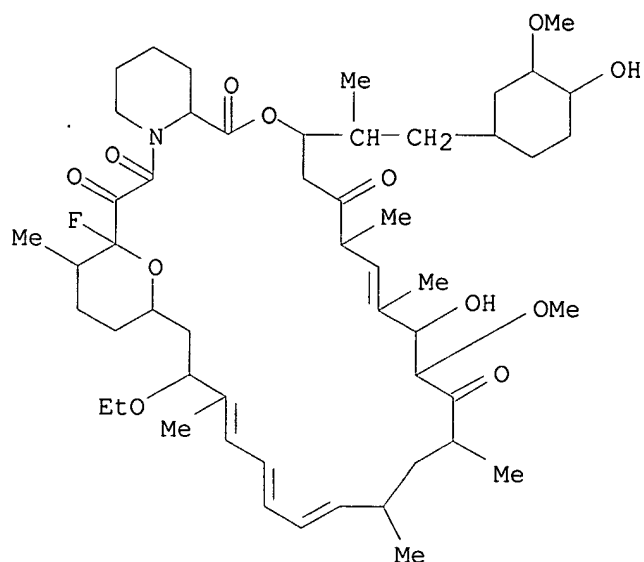


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:112371

L83 ANSWER 90 OF 166 REGISTRY COPYRIGHT 2006 ACS on STN
RN **232592-13-1** REGISTRY
ED Entered STN: 13 Aug 1999
CN Rapamycin, 7-O-demethyl-14-deoxy-7-O-ethyl-14-fluoro-, (7R)- (9CI) (CA
INDEX NAME)
FS STEREOSEARCH
MF C52 H80 F N O12
SR CA
LC STN Files: CA, CAPLUS

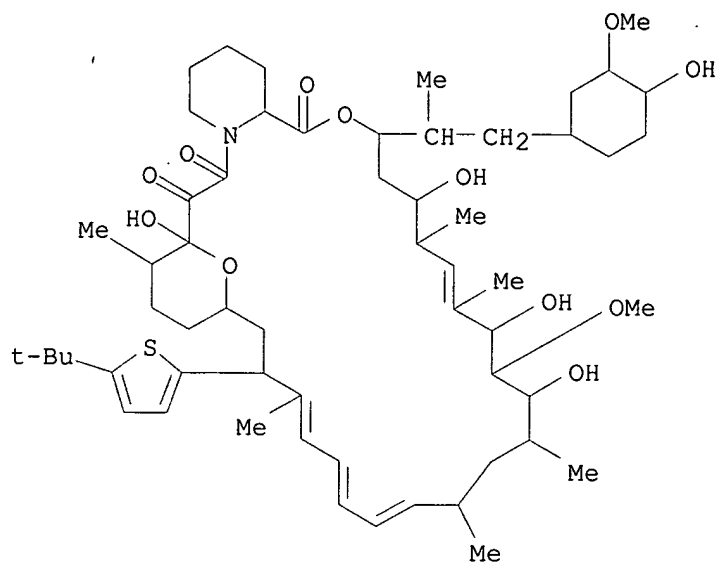


PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:112371

L83 ANSWER 100 OF 166 REGISTRY COPYRIGHT 2006 ACS on STN
RN **232592-02-8** REGISTRY
ED Entered STN: 13 Aug 1999
CN Rapamycin, 7-demethoxy-27,33-dideoxo-7-[5-(1,1-dimethylethyl)-2-thienyl]-
27,33-dihydroxy-, (7R,27S,33S)- (9CI) (CA INDEX NAME)
FS STEREOSEARCH
MF C58 H91 N O12 S
SR CA
LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)

1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:112371

L83 ANSWER 110 OF 166 REGISTRY COPYRIGHT 2006 ACS on STN

RN **232591-91-2** REGISTRY

ED Entered STN: 13 Aug 1999

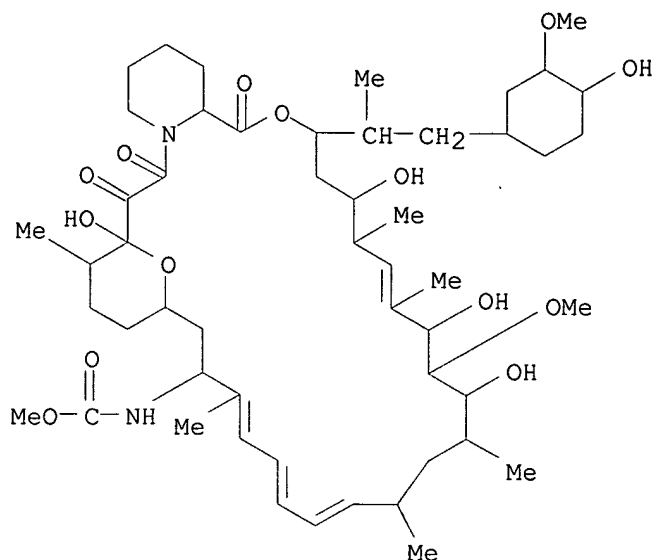
CN Rapamycin, 7-demethoxy-27,33-dideoxo-27,33-dihydroxy-7-
[(methoxycarbonyl)amino]-, (27S,33S)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C52 H84 N2 O14

SR CA

LC STN Files: CA, CAPLUS



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

1 REFERENCES IN FILE CA (1907 TO DATE)
1 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 131:112371

L83 ANSWER 120 OF 166 REGISTRY COPYRIGHT 2006 ACS on STN

RN **202522-60-9** REGISTRY

ED Entered STN: 12 Mar 1998

CN Rapamycin, 7-demethoxy-27,33-dideoxo-7-(2,4-dimethoxyphenyl)-27,33-dihydroxy-, (27S,33S)- (9CI) (CA INDEX NAME)

OTHER NAMES:

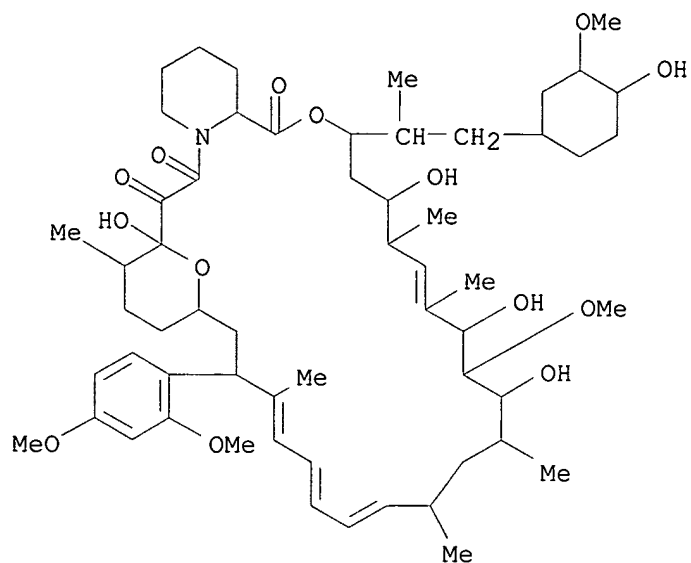
CN 23,27-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclohentriacontine-1,28,29(31H)-trione, 21-(2,4-dimethoxyphenyl)-4,5,6,9,10,11,12,13,14,21,22,23,24,25,26,27,32,33,34,34a-eicosahydro-5,9,11,27-tetrahydroxy-3-[2-(4-hydroxy-3-methoxycyclohexyl)-1-methylethyl]-10-methoxy-6,8,12,14,20,26-hexamethyl-, [3S-[3R*[S*(1R*,3S*,4S*)],5R*,6S*,7E,9S*,10R*,11R*,12S*,14R*,15E,17E,19E,21R*,23R

FS STEREOSEARCH

MF C58 H89 N O14

SR CA

LC STN Files: CA, CAPLUS, USPAT2, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)

3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:173056

REFERENCE 2: 131:112371

REFERENCE 3: 128:153966

L83 ANSWER 130 OF 166 REGISTRY COPYRIGHT 2006 ACS on STN

RN **186794-97-8** REGISTRY

ED Entered STN: 07 Mar 1997

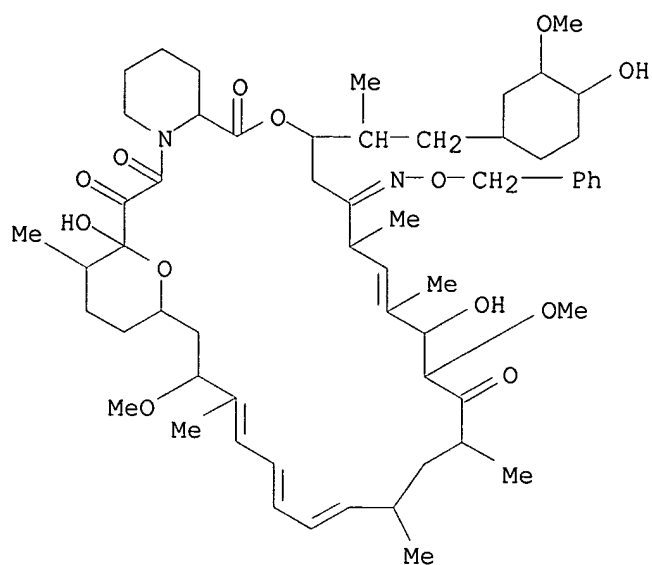
CN Rapamycin, 27-[O-(phenylmethyl)oxime], (27Z)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C58 H86 N2 O13

SR CA

LC STN Files: CA, CAPLUS, USPAT2, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:173056

REFERENCE 2: 131:112371

REFERENCE 3: 128:153966

REFERENCE 4: 126:153650

L83 ANSWER 140 OF 166 REGISTRY COPYRIGHT 2006 ACS on STN

RN **186757-68-6** REGISTRY

ED Entered STN: 06 Mar 1997

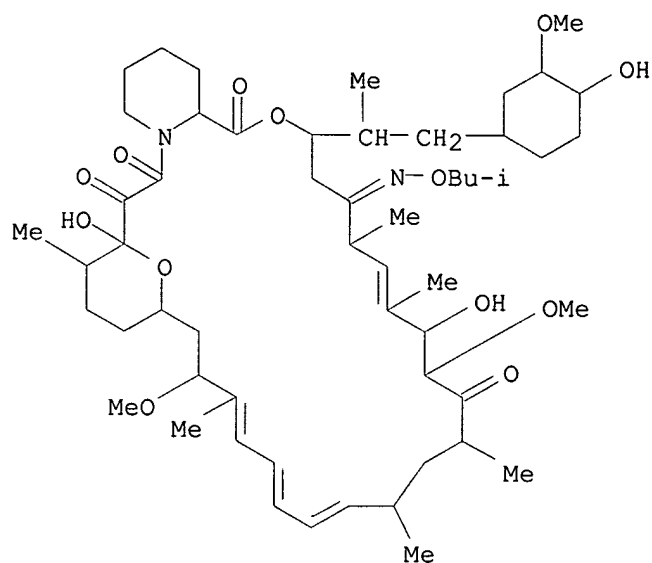
CN Rapamycin, 27-[O-(2-methylpropyl)oxime], (27E)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C55 H88 N2 O13

SR CA

LC STN Files: CA, CAPLUS, USPAT2, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)

4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:173056

REFERENCE 2: 131:112371

REFERENCE 3: 128:153966

REFERENCE 4: 126:153650

L83 ANSWER 150 OF 166 REGISTRY COPYRIGHT 2006 ACS on STN

RN 160401-32-1 REGISTRY

ED Entered STN: 26 Jan 1995

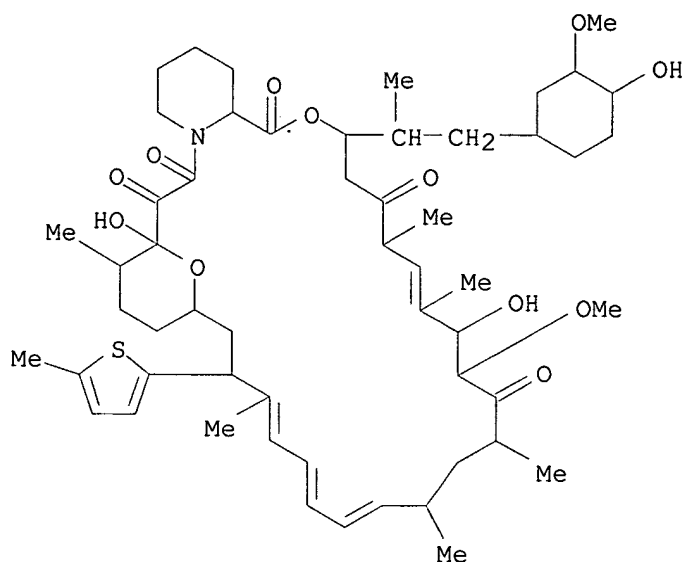
CN Rapamycin, 7-demethoxy-7-(5-methyl-2-thienyl)-, (7R)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C55 H81 N O12 S

SR CA

LC STN Files: CA, CAPLUS, CASREACT, USPAT2, USPATFULL



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

4 REFERENCES IN FILE CA (1907 TO DATE)
4 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 134:173056

REFERENCE 2: 131:112371

REFERENCE 3: 128:153966

REFERENCE 4: 122:80952

L83 ANSWER 160 OF 166 REGISTRY COPYRIGHT 2006 ACS on STN

RN **153984-91-9** REGISTRY

ED Entered STN: 30 Mar 1994

CN Rapamycin, 27-[O-(carboxymethyl)oxime] (9CI) (CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 23,27-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclohentriacontine, rapamycin deriv.

FS STEREOSEARCH

MF C53 H82 N2 O15

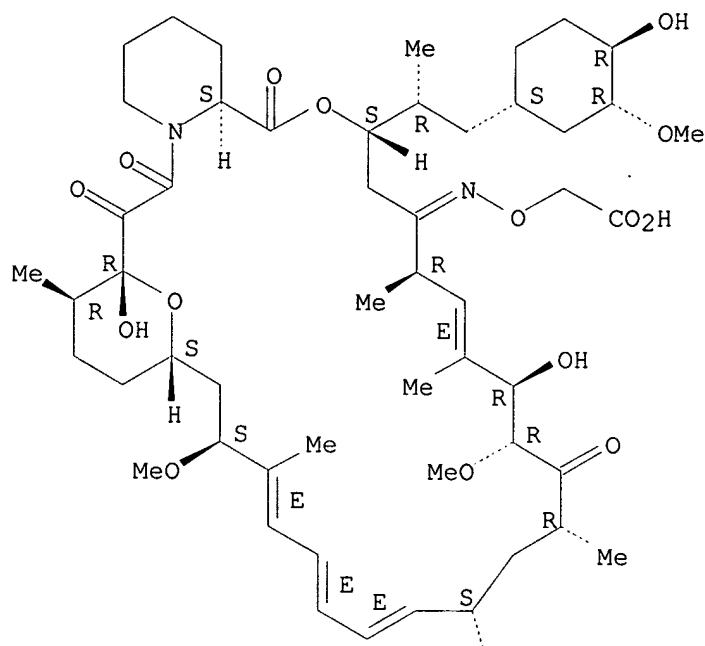
SR CA

LC STN Files: CA, CAPLUS, USPAT2, USPATFULL

Absolute stereochemistry.

Double bond geometry as described by E or Z.

PAGE 1-A



PAGE 2-A

Me

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3 REFERENCES IN FILE CA (1907 TO DATE)

3 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 122:213858

REFERENCE 2: 122:123081

REFERENCE 3: 120:212008

L83 ANSWER 166 OF 166 REGISTRY COPYRIGHT 2006 ACS on STN

RN 53123-88-9 REGISTRY

ED Entered STN: 16 Nov 1984

CN	Rapamycin (9CI)	(CA INDEX NAME)

OTHER CA INDEX NAMES:

CN 23,27-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclohentriacontine, rapamycin deriv.

OTHER NAMES:

CN (-)-Rapamycin

CN (3S, 6R, 7E, 9R, 10R, 12R, 14S, 15E, 17E, 19E, 21S, 23S, 26R, 27R, 34aS) - 9, 10, 12, 13, 14, 21, 22, 23, 24, 25, 26, 27, 32, 33, 34, 34a-Hexadecahydro-9, 27-dihydroxy-3-[(1R)-2-[(1S, 3R, 4R)-4-hydroxy-3-methoxycyclohexyl]-1-

methylethyl]-10,21-dimethoxy-6,8,12,14,20,26-hexamethyl-23,27-epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclohentriacontine-1,5,11,28,29(4H,6H,31H)-pentone

CN 23,27-Epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclohentriacontine-1,5,11,28,29(4H,6H,31H)-pentone, 9,10,12,13,14,21,22,23,24,25,26,27,32,33,34,34a-hexadecahydro-9,27-dihydroxy-3-[2-(4-hydroxy-3-methoxycyclohexyl)-1-methylethyl]-10,21-dimethoxy-6,8,12,14,20,26-hexamethyl-, [3S-[3R*[S*(1R*,3S*,4S*)],6S*,7E,9S*,10S*,12S*,14R*,15E,17E,19E,21R*,23R*,26S*,27S*,34aR*]]-

CN Antibiotic AY 22989

CN AY 22989

CN NSC 226080

CN RAPA

CN Rapammune

CN Rapamune

CN RPM

CN SIIA 9268A

CN Sirolimus

CN Wy 090217

CN [3S-[3R*[S*(1R*,3S*,4S*)],6S*,7E,9S*,10S*,12S*,14R*,15E,17E,19E,21R*,23R*,26S*,27S*,34aR*]]-9,10,12,13,14,21,22,23,24,25,26,27,32,33,34,34a-Hexadecahydro-9,27-dihydroxy-3-[2-(4-hydroxy-3-methoxycyclohexyl)-1-methylethyl]-10,21-dimethoxy-6,8,12,14,20,26-hexamethyl-23,27-epoxy-3H-pyrido[2,1-c][1,4]oxaazacyclohentriacontine-1,5,11,28,29(4H,6H,31H)-pentone

FS STEREOSEARCH

MF C51 H79 N O13

CI COM

LC STN Files: ADISINSIGHT, ADISNEWS, AGRICOLA, ANABSTR, BEILSTEIN*, BIOSIS, BIOTECHNO, CA, CAPLUS, CASREACT, CHEMCATS, CHEMINFORMRX, CIN, CSCHEM, DDFU, DIOGENES, DRUGU, EMBASE, HSDB*, IFICDB, IFIPAT, IFIUDB, IMSDRUGNEWS, IMSPATENTS, IMSRESEARCH, IPA, MEDLINE, MRCK*, MSDS-OHS, NAPRALERT, PATDPASPC, PHAR, PROMT, PROUSDDR, PS, RTECS*, SYNTHLINE, TOXCENTER, USAN, USPAT2, USPATFULL, VETU

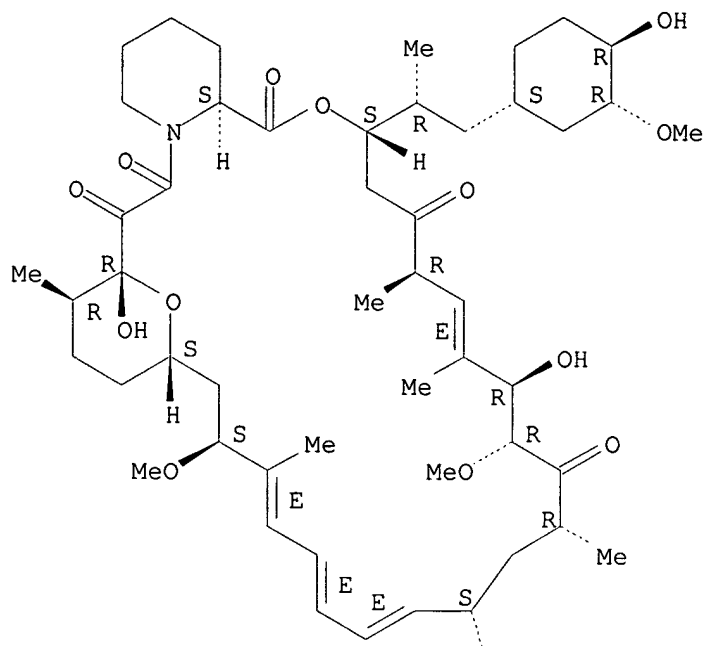
(*File contains numerically searchable property data)

Other Sources: WHO

Absolute stereochemistry.

Double bond geometry as shown.

PAGE 1-A



PAGE 2-A

Me

PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

3277 REFERENCES IN FILE CA (1907 TO DATE)
 184 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
 3295 REFERENCES IN FILE CAPLUS (1907 TO DATE)

REFERENCE 1: 144:114563
 REFERENCE 2: 144:114428
 REFERENCE 3: 144:114422
 REFERENCE 4: 144:114421
 REFERENCE 5: 144:108223
 REFERENCE 6: 144:106584
 REFERENCE 7: 144:104603
 REFERENCE 8: 144:101016
 REFERENCE 9: 144:100672

REFERENCE 10: 144:100651

=> d his

(FILE 'HOME' ENTERED AT 06:27:59 ON 09 FEB 2006)
SET COST OFF

FILE 'HCAPLUS' ENTERED AT 06:28:46 ON 09 FEB 2006

L1 2 S US20040082515/PN OR US2003-716062#/AP,PRN
E CLACKSON T/AU
L2 57 S E3,E5-E9
E GILMAN M/AU
L3 74 S E3,E8,E15,E17,E18
E HOLT D/AU
L4 36 S E3,E4
L5 103 S E45-E48
E KEENAN T/AU
L6 46 S E3,E12-E14
E ROZAMUS L/AU
L7 25 S E3-E6
E YANG W/AU
L8 1052 S E3-E30
L9 448 S YANG WU?/AU
E ARIAD/PA,CS
L10 185 S E3-E29
SEL RN L1

FILE 'REGISTRY' ENTERED AT 06:31:55 ON 09 FEB 2006

L11 133 S E1-E133
E NC4-OC5-NC2OC21OC3/ES
L12 9 S E3
E NC5-OC5-NC2OC21OC3/ES
L13 1186 S E3
L14 8 S L12 NOT RPS/CI
L15 1185 S L13 NOT RPS/CI
L16 37 S L11 AND L14,L15
L17 24 S L11 NOT (L16 OR SQL/FA)
L18 13 S L17 AND NR>=3
L19 11 S L18 AND NC5-OC5-NC2OC13OC3/ES
L20 72 S L11 NOT L16-L19

FILE 'HCAPLUS' ENTERED AT 06:45:55 ON 09 FEB 2006

L21 10 S L14
L22 3544 S L15
L23 3298 S L16
L24 3547 S L21-L23
L25 892 S L24 AND (PY<=1996 OR PRY<=1996 OR AY<=1996)
L26 17 S L1-L10 AND L25
L27 827 S L25 AND (GENETIC? OR BIOMOLECUL? OR BIOCHEM?)/SC,SX
E CHIMER/CT
L28 5671 S E11-E19
E E11+ALL
L29 11128 S E3+OLD,NT
E E18+ALL
L30 6790 S E1+OLD,NT
E CHIMERIC PROTEIN/CT
E E8+ALL
L31 17057 S E2


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L32      20620 S E2+ALL
           E E2+OLD,NT
           E FUSION/CT
L33      1 S E33
L34      17058 S E34-E52
           E PROTEIN MOTIF/CT
L35      66071 S E4-E40
           E E4+ALL
L36      69084 S E4+NT
           E GENETIC ENGINEERING/CT
           E E3+ALL
L37      103253 S E2+NT
L38      5093 S E18+OLD,NT
           E E1+ALL
L39      346300 S E1+NT
L40      130625 S E93(L)EXPRESS?
           E DNA/CT
L41      331318 S E3+OLD,NT
           E E3+ALL
L42      742161 S E3+OLD,NT OR E171+OLD,NT OR E172+OLD,NT OR E173+OLD,NT
           E CELL PROLIFERATION/CT
L43      78464 S E3-E11
           E E3+ALL
           E RECOMBIN/CT
L44      46528 S E49-E77
           E E49+ALL
L45      47814 S E1+NT
L46      87446 S E7+OLD,NT OR E9+OLD,NT
           E E9+ALL
           E HYBRIDIZATION/CT
           E E3+ALL
L47      82 S E1
           E E4+ALL
L48      51541 S E2+OLD,NT OR E11+OLD,NT
           E E11+ALL
L49      29988 S E3+OLD,NT
L50      16490 S E21+OLD,NT
L51      132 S L27 AND L28-L50
L52      33 S L51 AND (FKBP OR FRB)
L53      83 S L51 AND (FK506? OR FK 506)
L54      33 S L52 AND L53
L55      33 S L52,L54

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FILE 'REGISTRY' ENTERED AT 07:04:29 ON 09 FEB 2006

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L56      1 S RAPAMYCIN/CN
L57      1192 S L14,L15,L16 NOT L56

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FILE 'HCAPLUS' ENTERED AT 07:04:56 ON 09 FEB 2006

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L58      666 S L57
L59      152 S L58 AND (PY<=1996 OR PRY<=1996 OR AY<=1996)
L60      10 S L59 AND L28-L50
L61      139 S L59 AND (GENETIC? OR BIOMOLECUL? OR BIOCHEM?)/SC,SX
L62      8 S L60 AND L61
L63      18 S L1-L10 AND L58
L64      11 S L59 AND L63
L65      11 S L64 AND L60-L62
           SEL DN AN 3 5 6 7 8 9
L66      5 S L65 NOT E1-E18
L67      3 S L66 NOT PREPARATION/TI
L68      5 S L62 NOT L64

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L69 3 S L68 AND (PROTEIN? OR DEOXYRIBONUCLEIC? OR RIBONUCLEIC?)/CW,C
L70 2 S L69 NOT CYCLOPHILINS
L71 9 S L60,L63 NOT L64-L70
SEL AN DN 3 8
L72 2 S L71 AND E19-E24
L73 13 S L59 AND (?FKBP? OR FRB?)
L74 5 S L73 AND L67,L70,L72
L75 8 S L73 NOT L74
L76 7 S L67,L70,L72,L74
L77 6 S L76 NOT 142:291846/DN
L78 6 S L59 AND (FUSION OR ?CHIMER?)
L79 5 S L78 NOT 143:32417/DN
L80 6 S L77,L79
L81 6 S L80 AND L1-L10,L21-L55,L58-L80
L82 6 S L81 AND (FUSION OR ?CHIMER? OR ?PROTEIN? OR ?PEPTIDE? OR BIND
SEL HIT RN

FILE 'REGISTRY' ENTERED AT 07:21:05 ON 09 FEB 2006

L83 166 S E25-E190
SAV L83 SCHLAP716/A
L84 1193 S L14-L16
SAV L84 SCHLAP716A/A

FILE 'HCAPLUS' ENTERED AT 07:22:03 ON 09 FEB 2006

FILE 'REGISTRY' ENTERED AT 07:22:43 ON 09 FEB 2006

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